NOV 4 1947

Vol. 106
No. 2757

Pages 405-430

October 31, 1947

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Science

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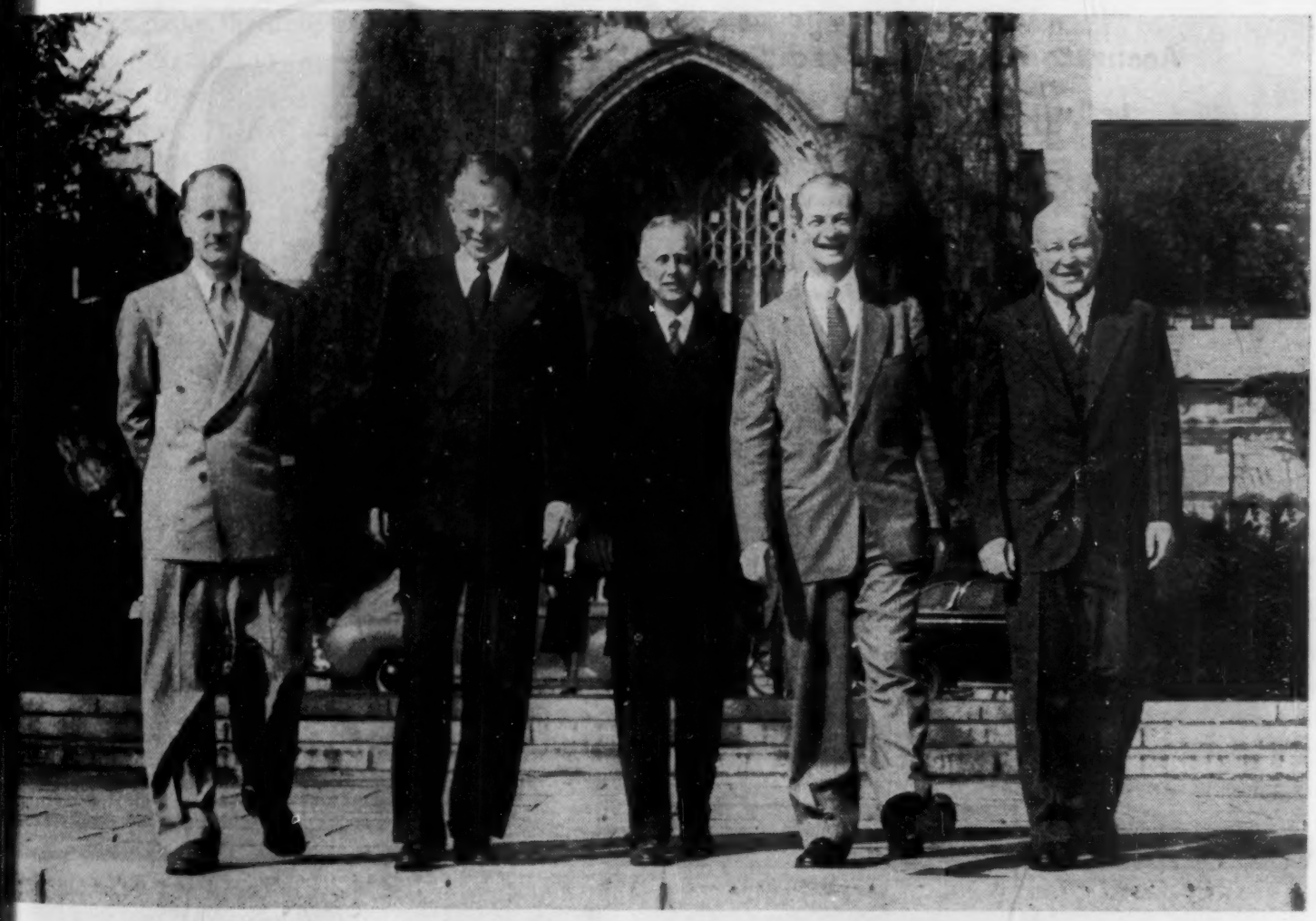

The four Silliman Lecturers who gave principal addresses during Yale University's Sheffield Scientific School Centennial pictured with the director of the School in front of Sterling Memorial Library. *Left to right:* George W. Beadle, biologist, California Institute of Technology; Ernest O. Lawrence, physicist, University of California; Edmund W. Sinnott, director of the School; Linus C. Pauling, chemist, California Institute of Technology; and Wendell M. Stanley, pioneer in the field of virus research, Rockefeller Institute for Medical Research.

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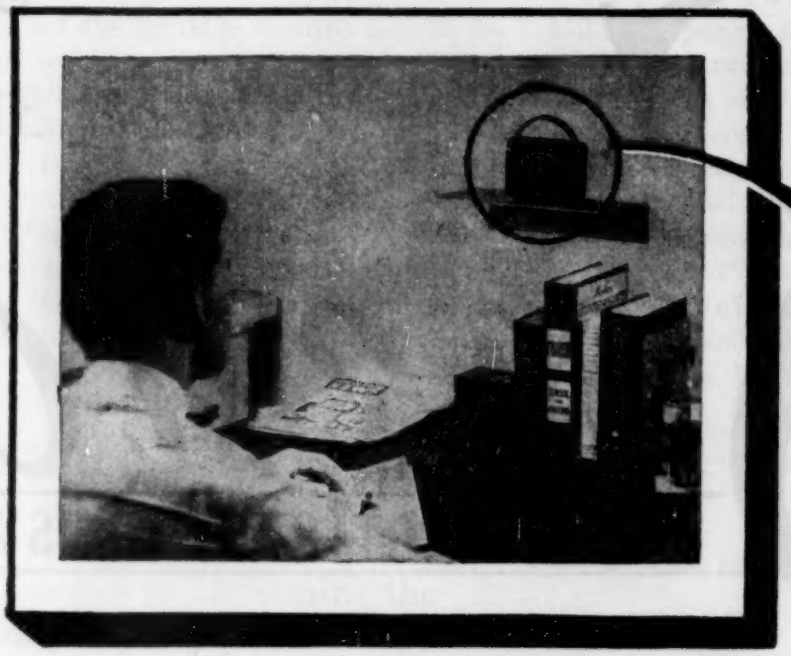

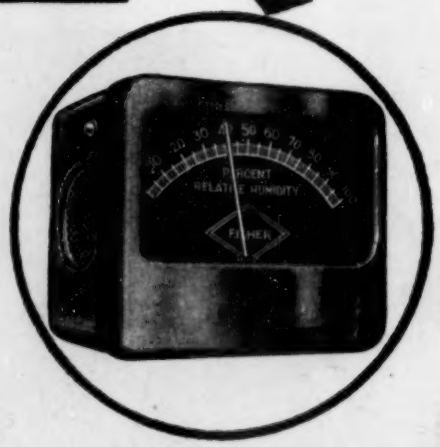

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Some Problems of Human Ecology in Polar Regions

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THE PROBLEMS OF MAN IN THE ARCTIC and Antarctic are under examination by many. These are of special interest to the ecologist or environmental physiologist.

The field of interest of the environmental physiologist can be briefly described as the reactions of normal man to the complex of natural and artificial factors of the environment. Physiology is the study of function of living matter. It includes the study of the human organism, an exquisitely integrated mechanism, the behavior of which is essentially the summation of actions and interactions of a mass of living cells, of groups of specialized cells called tissues, of combinations of tissues to make body organs; of body organ systems, of the organism as a whole, and of the interrelation of organisms (men). These reactions and interactions are continually influenced by physical, chemical, and emotional factors of the environment—internal and external.

The environment includes everything, and at the technological level of our present-day culture, with its dependence upon highly complicated machinery, with extremely artificial environments of technical and industrial areas, and with means of transport so rapid that man can be moved within an hour from desert torridity of 135°F. to the frigidness of the stratosphere of 65° below zero, the extreme range of physical impacts which confront man has no counterpart in history.

In spite of our superb machine and engineering developments, man in the final analysis, and man alone, is the focal unit of our functional society. Men, not machines, make our Nation.

The basic interest of the human ecologist is the study and understanding of the responses of the normal man to the multiplex factors of climate, cloister, and clothing, of factory, field, and fairway.

The polar regions are frontiers for investigation of descriptive natural sciences. They are also regions which offer unlimited opportunity for the integration of the man's capabilities and limitations with engineering design and development. The areas demand a continuing concern of man's reactions to the environments by the engineer, the economist, the geographer, and frontiersman; they demand a continuing concern of the geographical parameters of the physical and biological factors by the biologist, the engineer, the community planners.

In March 1946, the Arctic Institute of North America published Bulletin No. 1, entitled, *A program of desirable scientific investigations in Arctic North America,* a statement which was presented in the hope that it might serve as a working agenda and as a guide in planning a comprehensive program of Arctic research in North America. By design, problems related to human biology, including medicine, were omitted.

An outline of a program for similar research, but in the fields of human biology, is presented in this paper in order to invite comment and to indicate directions which the study of man in polar areas may take. A large section of this program applies only to the Arctic; the fundamental differences between the Arctic and Antarctic in regard to the habitability and inhabitation are the essential basis for this orientation.

It should also be noted that investigations are included which deal specifically with physical factors of the environment. The study and understanding of these are essential for the evaluation of man's reactions to the environment. Their inclusion in this biological program emphasizes the need for close integration of all fields of study when an analysis of the polar regions is made.

The first problems which will be considered can be grouped under the heading of *personnel.* These encompass the establishment of criteria for selection of persons to be engaged in polar work (and thereby, of course, the establishment of the validity of selection) and the study of needs and methods for special training and selection.

An approach to the selection requirements upon which to base the choice of personnel for Arctic service can be made through the study of present inhabitants. The motivations, personalities, and adjustments of men and women who have gone into the Arctic, and stayed or returned after a period, can supply a basic amount of generalized data for most types of duties which might be expected in military or civilian colonization of the North. The study of groups such as exist in villages or towns and in mining and lumbering camps can reveal significant comparative information which may be related to selection of personnel for establishing large aerodromes, camps, or colonies. The hunter-trapper personality may suggest standards for the selection of isolated outpost personnel like that needed for radio stations, emergency

The opinions expressed in this article are the author's and do not constitute official opinion of the Navy Department.

airfields, and ranger posts. The crews of a number of small Arctic trade and cargo vessels which ply the polar fringe seas may be fair sample material for basing selective methods for men to be assigned such duty if the demand becomes greater. A psychological evaluation of the bush pilot, one of the outstanding groups of present-day pioneers, should give an extremely valuable picture which could find ready translation to selection of North country pilots.

It is probable that in many instances the population sample will be inadequate for a complete study; nevertheless, initial directions should evolve from the analysis of present inhabitants. Assuming that the psychosocial study of present non-native Arctic populations reveals the existence of selective characteristics which can be generalized, then the establishment of criteria for selection of personnel for Arctic service (civil and military) will naturally permit a series of validating experiments only if selectees or volunteers for service in the Arctic are available. Government channels, again including military and nonmilitary personnel, will be the potential source.

In the course of establishing the need for preselection (and selection) standards and the validation of criteria for selection, a number of important correlations should be explored. The "traditional" emotional disturbance associated with Arctic isolation will demand reexamination. No doubt can be raised regarding the fact that some men cannot tolerate "Arctic isolation," but there is no evidence which clearly associates the development of the instability with the Arctic rather than with the isolation. If both factors are involved, there are as yet no data for assigning relative weights to each.

These broad psychosocial studies should also permit the investigation of two other areas of interest: the relationship of an experiential component of personal history with adjustment to Arctic service, and the relationship of motivation to emotional stability. Many persons who have never seen the Arctic have experienced conditions and situations as severe as, or even more severe than, those encountered in the upper latitudes. How residents of the Dakotas, Montana, Idaho, and some provinces of Canada compare in their adjustment to the Floridian and Californian should be of interest. It must be recalled that many Arctic whaling ships were manned by West Indians, Portuguese, and Mediterranean natives; and of the five men who reached the North Pole with Peary, four were Eskimos and one, Matthew Henson, was a Negro.

As for motivation in relation to adjustment to the Arctic, history is heavy with the achievements against adversity by highly enthusiastic explorers. There is little basis for suspecting factors of the Arctic which might tend to mitigate the forcefulness of motivation in overcoming difficulties, real or imaginary.

The development of methods of training and indoctrination of candidates for Arctic service offers a challenging field for educators who are interested in two rather diverse problems. The simpler is training by methods of simulation (artificially reproduced situations which can be controlled). The evolution of satisfactory methods for simulated training for Arctic jobs, whether engineering, farming, maritime, or community planning, should result in accelerated and economical preparation of men and women for Arctic service. For actual field training to begin with the primer problems is costly and inefficient.

A challenge greater than the simulated training is the indoctrinational program. Few areas of importance have a greater lore of fable than the Arctic, and generally well-informed persons are either uninformed about the Arctic or, even worse, ill informed. A program for indoctrinating people about the Arctic will, perforce, require not only the learning of facts but also the unlearning of fiction. In spite of our inheritance of information, the Arctic Circle does not demark the Arctic, the Arctic is not characterized by six months daylight and six months darkness, the lowest temperatures recorded on the earth are not in the Arctic, and Eskimos do not generally trade wives.

To the educational research in methods for simulated training and for indoctrination should be added research to develop effective survival teaching. Although this may be of primary importance to limited military groups, it should find broad application for transpolar air travelers, crew and passengers alike. Emergency landings in the Arctic are relatively safe compared to those on open seas; nevertheless, a basic understanding of survival methods is essential.

Another large field in need of investigation is related to *factors of the environment*. As indicated earlier, although this is a discussion of a program in human biology, the ecologist must make a critical examination of the physical as well as the biological factors. It will be clear that many physical assays of the environment which are proposed for study in the polar regions are also unknown for temperate zones. In the polar areas, the impact of these factors are so sharp that the biologist must have a clear picture of all the physical factors of the environment. The relation of some of the factors to biological problems will be commented upon in some instances, but a thorough development of this thesis cannot be made here.

The study of meteorological factors is of import; and the relationship to climate is obvious. Polar meteorology for the biologist must be a long-term, continuing study and must be carried out at an adequate network of observatories. In spite of a common tendency to think of polar meteorology as homogeneous, the fact remains that the range is great and the heterogeneity is general.

The physical measurement of solar radiation is essentially a problem of geophysics. But the importance of knowing the spectral range and the intensities of radiant energies in the polar regions warrants an active interest by the physiologist. Such radiant energy is highly com-

plex and variable, for it may originate from direct sunlight and from light that is either diffuse or reflected, or from snow or ice, or it may be refracted from vapor. Polar mirages, sky maps, effects of snow-polarized light, and intensity of total lunar and stellar light for winter activity have to be studied.

Sound and noise levels may be so low that footsteps on the snow several hundred yards away are audible; or they may be of unearthly magnitude when pack ice is breaking up, churning and crashing.

Against quietude, the shrill call of the loon is enervating. Background noises, such as special sound of winds, aircraft, tractors, and the like in the low temperature of polar winters, have not been measured.

Physical phenomena, such as cosmic rays, aurora, and geomagnetism, are of significant interest to the geophysicist. His findings may be worth the attention of the physiologist, but the field is unexplored.

Humidity, fog, icing conditions, winds, water currents, ice, snow, topography, terrain, barometric pressure, and similar factors influence biological behavior. The study of the effects of these conditions on the organism cannot be logically pursued until the values of the factor are ascertained. Again, one must warn against assuming or expecting uniformity throughout polar regions. Not only are the Arctic and Antarctic very different in many respects, notably with respect to mean altitude of land surfaces, but also various parts of the Arctic may differ in almost all regards, except for the few or even for the single character chosen to define the entire polar region.

The assay of biological factors of polar environment will find its greatest share of interest in the Arctic since, except for fringe waters, the Antarctic, like the Greenland Ice Cap, is quite devoid of life. The first phase of a bioassay of polar regions by the ecologist should be a climatological analysis. Systematic study of climatic factors for the various polar areas is being pursued, but on far too modest a scale to allow a clearly defined presentation of Arctic and Antarctic climates.

The strict study of flora and fauna, which may fall more clearly to the plant and animal biologist, has had a share of attention, but, as indicated in the program of the Arctic Institute of North America (Bulletin No. 1), a great deal is yet to be investigated. The study of animal and plant life in the polar regions having environmental impact on man can be carried on almost without limit.

Bacteriological aspects of these geographical areas present a challenging opportunity. It is known that bacterial processes are retarded, but whether this is due entirely to temperature factors is not clear. Surveys of the bacterial content of the air, soil, snow, ice, inland waters, and sea should be conducted. The metabolism of the bacteria which are indigenous in the polar regions, their culture characteristics, and their pathogenicity (or nonpathogenicity) offer the field-minded bacteriologist and the human ecologist an intriguing problem.

The study of the extent, behavior, growth, and reproduction characteristics of the insect populations in the Arctic will afford valuable information for the control of the pestiferous insects like the Arctic mosquito and sand flies, but even more, it may offer a field for studying basic biological processes under special natural environments. A fundamental approach to relation of environment to genetic changes is being carried on by a study of the *Colias* in the Arctic by W. Hovanitz (personal communication).

Although an exhaustive search of the literature has not been made, the writer believes that no virological survey of the Arctic has been conducted. The environmental physiologist will be interested in such investigations.

Both the botanist and the ornithologist have been in the field, and of all the special phases of biology these two have carried out the most work; the greatest share of this has been descriptive, however, and there is, as with animal forms, a potential wealth of information regarding the physiology of polar plant life.

The rewards to the human ecologist for interest in Arctic vegetation can be found in regard to nutritional value of the vegetation, toxins, fuel utilization, cultivative potential, and even pharmaceuticals.

Mammals have been of economic interest, mostly for pelts and in some few instances for food. Scientific inventory and population analysis on a large scale should be of interest with respect to food, fur, domestication, pack and work use (dogs, reindeer, ponies), species balance, and basic animal ecology. It is interesting to note in passing that animal trails or runs across permafrost (permanently frozen ground) influence the permafrost character by the wearing off of the top insulating grasses.

It should be emphasized that the comments regarding plant and animal life are made with reference to the biological status of the polar regions to the extent that they constitute a series of factors of man's environment. The natural habits of the mosquito in the Arctic are of intrinsic interest, but the mosquito problem, as pest or potential disease vector or for control and irradication, is the one posed in this paper. The behavior of bacteria in Arctic regions is a challenging study, but the problem herein presented is mainly bacteria (pathogenic and nonpathogenic) as they constitute a factor of the environment.

A third general field in need of investigation in polar regions is *health and sickness*. Most of this work is pointed to the upper latitudes, since human inhabitation of the Antarctic continent is limited to explorers. The study of health of the native and the long-time white resident (trader, missionary, bush pilot, trapper, and civil servant) has been touched but very slightly. Medicoethnological studies have been conducted in limited phases, chiefly dental, general dietary, and some infectious diseases, but a critical and extensive examination of the historical aspects of the health status has yet to be made. The medical observations incorporated in the writings of early

explorers and travelers have not been assimilated in a single body of information.

More attention is now being directed by governmental agencies to medical studies associated with Arctic and sub-Arctic regions, e.g. by the Interior Department in Alaska, by the Department of Mines and Resources in Canada, by the Danish Government in Greenland, and by the Northern Sea Route Administration in the Arctic and sub-Arctic USSR. The data, however, are still meager and sporadic. Public health surveys have concentrated heavily on tuberculosis; but the field is open for thorough and extensive disease surveys and control, medical requirements, and medical climatology and geomedicine.

From the purely medical viewpoint, the Arctic offers an extremely fertile field of inquiry regarding epidemiology, incidence, mortality, and morbidity of many diseases. The nutritional aspects of the Arctic population and the study of contagious diseases, endemic and epidemic, of diseases and natural growth of childhood and adolescence, of cancer, and, of course, longevity constitute a small share of the problems still unsolved. Hypertension, and cardiovascular disease in general, has reportedly a very low incidence, but precise data are not readily available. Most specialties of medicine such as dermatology, internal medicine, endocrinology, ophthalmology, gynecology, and urology will find interesting data when the native and the long-time immigrant population is studied. The responses of newcomers to the Arctic should reveal data pertinent, not alone to the specific disease groups, but also to the general aspects of physiological adjustment.

Some specific diseases which may be of interest to the field of Arctic or polar medicine will include pneumonia, tuberculosis, typhoid fever, rheumatic fever, allergy, arthritis, nephrosis, myositis, chilblain, frostbite, and snow blindness.

Because of the relatively limited population and the capacity to isolate whole villages, the work of the Public Health doctor, especially in Greenland, has been effective and instructive and, when accepted as an example to indicate potential fields of inquiry, is most stimulating.

We pass now from our consideration of the general medical and health status evaluations of the peoples of the Arctic to more specific *physiological problems* which are in need of investigation. First are those related to the assessment of health in the polar regions. Longitudinal studies—that is, long-term studies conducted on individuals over a significant part of their growth or longevity periods, rather than short-term studies of many persons of different age groups—will be revealing, especially in regard to the growth and development of the native. The physiologist interested in the child and adolescent has an opportunity to study not only growth in relation to nutrition (of different quality than temperate zones) and to special seasonal and climatic conditions, but also psychophysiological developments within a cultural group which treats its children with a real acceptance of the child as a person.

The physiology of adaptation or adjustment, or somatic learning, or even acclimatization is indeed a challenging problem, whether the process be real or imagined. The reactions of the organism, as a whole or as separate parts (as, for example, the peripheral vascular bed of weather-exposed parts of the body), to polar climatic factors have not been measured. The processes of wounding and wound healing, of disease susceptibility and recuperance, appear to be altered in polar regions. Critical evaluations have as yet to be made. It may be added that, although many physiological changes associated with lowered environmental temperature have been investigated, there are many factors of the polar environment in addition to temperature which may play significant roles. Actually as for temperature, indoor temperatures in the upper latitudes are usually maintained much higher than farther south; and outdoor clothing is usually adequate to keep northern residents more comfortable in below-zero weather than Eastern Seaboard inhabitants are likely to be in ordinary street clothing in above-zero winter weather.

An intriguing psychosomatic problem of Arctic life is the general acceptance of reality as a basis for behavior. Rigid schedules are not maintained, the elements of weather are not combatted, and, all in all, the pace shifts with the environmental factors. One should point out that this is a pattern of the native and long-time inhabitants and not necessarily true for the newcomer.

Some more specific physiological problems which present themselves include the effects of solar radiation (of polar intensity, range, and duration) on the eyes, skin, and body-temperature regulation; nutritional requirements for the low temperature and strenuous activity that are encountered on the trail; water balance among natives and white man; mineral balance, especially in the light of low salt contents; calcium source (in growing children); vitamin requirements; and the fat, protein, and carbohydrate relationships. In the case of these last problems the fish and meat-eating Eskimos of King William Island region offer a valuable source of information. In addition, postural gait and orthopedic studies in general will be interesting, for leather-arch supporting shoes are not used either by the natives or by the white man on the trail.

The cardiovascular balance of the polar inhabitants, kidney function, neuromuscular reactions, fitness in general, and psychomotor and sensory responses appear to warrant closer examination. It is not unreasonable to expect productive results from almost all phases of human physiological investigation which may be conducted on the inhabitants of the Arctic regions.

A very practical broad field of inquiry which involves the physiologist is that related to engineering, especially engineering in regard to man's employment of machine

or machines for man. In this area fall the problems of food, hygiene and sanitation, clothing, transportation, and community planning.

The *engineer-physiologist problems* regarding food (exclusive of the production of food that would be the province of the agricultural engineer) are related to food storage, processing for Arctic use, preparation, packaging, messing facilities, and special rations (pemmican and others) for emergency use. Problems in hygiene and sanitation include water supply, sewage disposal, housing (heating, ventilating, humidity control), laundry requirements, and the like. Humidity control in the dry, cold climates is an important problem, for in the usual condition which exists in northern houses the heated dry air causes the upper respiratory passages to become dehydrated. Not only is this very annoying, but it also makes one more sensitive to invasion of infectious agents when these agents happen.

The engineer-physiologist team must also attack problems of devising and improving transportation vehicles from the standpoints of operation design, maintenance convenience, and human factors in the vehicle design—heating, vibration control (for riding over rough tundra, sastrugi, and ice), noise elimination, removal of noxious gases, comfort, and safety aspects. The design and development of the best clothing for over-all use also demand the cooperation of the engineer and the physiologist.

Finally, for community planning, whether the community be a mining camp, an aerodrome, or a sizable village, the problems demand a combined attack by the human ecologist, the engineer, and the geographer.

To the writer, the essential and demanding requirement that the various disciplines of science and technology work together is one of the most exciting aspects of research in polar regions.

A System of Nomenclature for Isotopic Compounds

John W. Otvos and Charles D. Wagner
Shell Development Company, Emeryville, California

THE RAPIDLY INCREASING AVAILABILty of isotopes of the common elements, both iradioactive and stable, makes it a certainty that research studies will soon involve the synthesis and utilization of many compounds containing abnormal concentrations of isotopes, usually in definite positions in the molecules. At the present time there is no general system of nomenclature for such compounds (with the exception of those containing deuterium), and therefore they are identified by structural formulas and by textual description.

Deuterium compounds are named in this country by the modified Boughton system, this convention having been established by the American Chemical Society in cooperation with representatives of the American Physical Society (E. J. Crane. *Science*, July 27, 1934, pp. 86–89). Under this system of nomenclature the position and number of deuterium atoms in the molecule are indicated in the name itself by the suffix -m,n, . . .-d_r, where m and n are the positional numbers of deuterium atoms in the molecule or portion of the molecule and r is the number of deuterium atoms per molecule.

Several considerations seem pertinent concerning the establishment of a general system of nomenclature for isotopic compounds:

(1) The system of nomenclature should be applicable to all isotopes.

(2) For indexing purposes, as well as for clarity and convenience, the name of the isotopic compound should be very similar to that of the normal one.

(3) The position or positions in the molecule of the isotopes present in abnormal concentration should be indicated.

(4) Compounds containing isotopes in any abnormal concentration should be named by this system, rather than only those containing isotopes in essentially 100 per cent concentration, since for tracer purposes radioactive isotopes or stable isotopes in relatively small concentrations may be used.

The importance of point 4 is considerable. It is unlikely that isotopes other then deuterium will soon be available in high purity. Moreover, the ratios of isotopic masses of other elements are much smaller than the ratio of those of hydrogen. Any differences in physical properties or chemical reactivity between normal compounds and those containing pure isotopes of other elements would therefore be much less marked than the differences obtainable with hydrogen isotopes. As a consequence, interest in pure isotopes other than deuterium should be small. Yet the synthesis and use of isotopic compounds involve very specialized problems whether the compounds contain an isotope in 100 per cent purity or not, and convenient reference and indexing in all such cases will be important.

These ideas were probably considered by the American Chemical Society Committee on Nomenclature, Spelling, and Pronunciation, for in its report on nomenclature of deuterium compounds (E. J. Crane. *Ind. eng. Chem.* (News ed.) 1935, **13**, 200) this statement is made: "If compounds of tritium are eventually made, they can readily be named in like manner, 't' being used as is 'd'

in the Boughton names for deuterium compounds." Obviously, it is not inferred that such compounds would contain 100 per cent tritium atoms at a particular position in the molecule. It would seem entirely practical to name a compound to indicate abnormal isotopic concentrations and to specify the isotopic purity in the text in the same way that purities of ordinary chemical compounds are given.

As a beginning for consideration of the establishment of a general system of nomenclature for isotopic compounds, it is suggested that the system for deuterium compounds now in use in the United States be extended by using the suffix -m,n, . . . -i_r^p, where m and n are the positional numbers or Greek letters commonly used for indicating the locations of substituents (in this case used to indicate the positions of an isotope in the molecular skeleton), i is the element symbol in lower case letters[1] of the isotope in abnormal concentration, p is the mass number, and r is the number of atoms in the molecule containing abnormal concentrations of the isotope i^p. As with deuterium compounds, it may be necessary for clarity to follow names of atomic groupings (methyl, ethoxy, etc.) with the proposed suffix. A few examples of this system of nomenclature are shown in Table 1.

It will be seen that, in general, when the Geneva system of nomenclature applies, this system is applicable also. There are a few exceptions, such as the following:

$$C_6H_5N{=}N^{15}{-}C_6H_4Br$$

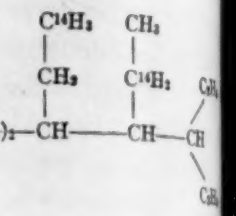
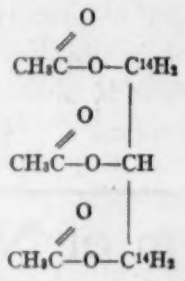
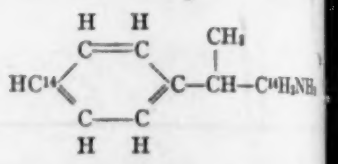
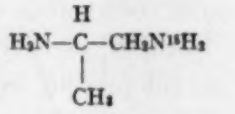
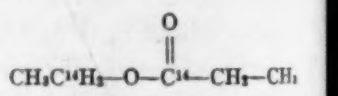
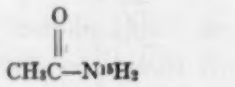
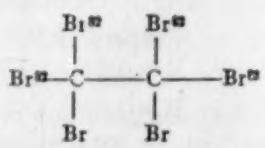
$$CH_3C(=O){-}O^{18}{-}C_2H_5$$

where one of two atoms of an element in a functional group is isotopic and the functional group is ordinarily expressed as a whole. These situations could perhaps be solved by extending the accepted system of nomenclature in some degree. For instance, the azo compound might be referred to as p-(phenylazo-α-n^{15})-bromobenzene and the ester as a ketone, methyl ethoxy-o^{18} ketone, hence

$$CH_3C(=O^{18}){-}OC_2H_5$$

would be methyl ethoxy ketone-o^{18}. However both of these instances, and particularly the second, involve fundamental departures from, or extensions of, the present nomenclature and are presented here only to demonstrate that solutions to such problems can doubtless be found.

TABLE 1
EXAMPLES OF NAMES OF ISOTOPIC COMPOUNDS

2-butene-1-c^{14}	$CH_3{-}CH{=}CH{-}C^{14}H_3$
2-propen-1-c^{13}-1-ol	$CH_2{=}CH{-}C^{13}H_2OH$
3-ethyl-4-(ethyl-α-c^{14})-5-(ethyl-β-c^{14})-octane	
1,2,3-triacetoxypropane-1,3-c^{14}	
β-phenyl-4-c^{14}-propyl-α-c^{14}-amine	
hexadecanoic-6-c^{14} acid	$CH_3(CH_2)_9C^{14}H_2(CH_2)_4COOH$
ethanoic-2-c^{13} acid (acetic-α-c^{13} acid)	$C^{13}H_3COOH$
1,2-propanediamine-1-n^{15}	
ethyl-α-c^{14} propanoate-1-c^{14}	
acetamide-n^{15}	
hexabromoethane-1,1,2,2-br_4^{82}	

1. The sixth compound above was recently referred to by long descriptive name: "hexadecanoic acid labeled at carbon atom six with carbon fourteen" (William G. Dauben. Abstracts, Atlantic City Meeting, American Chemical Society, April 1947, p. 5M).

2. The seventh compound above was recently referred to as "acetic acid containing isotopic carbon in the methyl group" (H. S. Anker. *J. Biol. Chem.*, 1946, **166**, 219).

3. The same principle could be applied to the new Dyson system of notation (G. Malcolm Dyson. Lecture, Royal Institute of Chemistry, London, 1946) for organic compounds, *i.e.* the isotope notation would immediately follow the "operation" which first refers to the atom or atoms in question. From our limited knowledge of the Dyson system it would appear that the use of a colon to set off the desired symbols is feasible. Thus, the third example above would be C8.3,4,5C2:11,14C14, the seventh would be C2:2C13.X, and the last would be C2.1,1,1,2,2,2BR:1,1,2,2BR82.

[1] Although the use of lower-case letters is consistent with the deuterium system of nomenclature, there is doubt in the minds of the authors as to whether the symbols of other elements should likewise be in lower-case letters, since this represents a more abrupt departure from convention. Also, confusion may result when lithium, lanthanum, or lutecium are involved, since a lower-case "l" may be confused with the numeral "1". However, this very departure may serve to draw attention to the fact that a special nomenclature is being used.

On the other hand, if a compound is generally referred to by a common name and cannot be conveniently characterized by the Geneva system, the use of the suggested nomenclature becomes simple only when the atoms of a particular element are isotopic in all positions of that element in the molecule. This situation will undoubtedly be frequent; some examples are: tyrosine-n^{15}, thyroxine-i_4^{131}, cystine-s_2^{35}, ergosterol-o^{18}, fructose 1,6-diphosphate-p_2^{32}.

It is hoped that these ideas will initiate further studies on this nomenclature problem so that publications in the near future which are concerned with isotopic compounds may be indexed conveniently and consistently.

NEWS *and Notes*

The fires which swept through Bar Harbor, Maine, this past week totally destroyed the Roscoe B. Jackson Memorial Laboratory for Cancer Research. C. C. Little, director of the Laboratory, reported to *Science* that the replacement value of the buildings, library, equipment, and mice is approximately $500,000. Little of this was covered by insurance. In addition to destruction of the Laboratory itself, the staff suffered almost complete loss of personal property. The summer student colony equipment was likewise consumed by the fire. An ABC announcement on Sunday, October 26, stated that the Damon Runyon Memorial Fund for Cancer Research is giving $50,000 immediately toward reconstruction work. Dr. Little indicated that less than 100 of the pedigreed mice were saved and that these are in scattered strains which cannot be identified. Because of exposure to fire and heat, those rescued are in very poor condition.

The staff is already making plans for renewing its work. Scientists everywhere may assist in rebuilding the library by sending pertinent reprints in the fields of genetics, embryology, cancer research, and experimental biology and medicine, and by advising the Laboratory about strains of mice from which extra litters are available for beginning the breeding work.

The Nobel Prize in Medicine was awarded jointly on October 23 to Carl F. Cori and his wife, Gerty T. Cori, of Washington University, St. Louis, and to Bernardo A. Houssay, of the Instituto de Biología y Medicina Experimental, Buenos Aires. The Coris, who received the Prize for their discovery of the "mechanism of enzymatic synthesis of glycogen, or animal starch" through the isolation of the enzyme, phosphorylase, are the third husband-wife team to be so honored, having been preceded by Pierre and Marie Curie (physics) and Frederick and Irene Curie Joliot (chemistry). Dr. Houssay, a diabetes specialist, who will receive half the Prize ($24,460.50), was honored for his "discovery of the significance of the hormone produced by the frontal lobe of the hypophysis."

AAAS–UNESCO Fellowships

These are anxious days for scientists. These are worried days for everybody who thinks about the future. The membership of the AAAS, the readers of this journal, know that everything possible should be done to maintain international peace and stability. Europe's economic distress, our own jittery struggle with prices and wages, our growing suspicions of Europe's policies and plans, and the feeling, in once friendly Europe, against "comfortable America" are bad, but still they are trivial compared with the social upheavals that would be inevitable throughout the world if a new bombing and poisoning war should build up out of international ill will and misunderstanding.

What can we do? We can work for international good will and tolerant understanding. Every group that has examined the situation reports that the liberal exchange of key personnel among the nations is one of the surest ways of attaining the goal. And scientific exchanges must rank high, because the scientist is so readily and naturally international and peacefully cooperative. The United Nations, UNESCO, the National Research Council's UNESCO Committee, the various associations of scientific workers, and many other groups are on record as to the high importance of scientific interchanges. Traveling politicians are frequently viewed with alarm; traveling merchants may be suspected of working for special interests rather than for the world at large. Scientists, scholars, and artists, however, are relatively clear of suspicion; they are heartily welcomed nearly everywhere.

I am inviting you to help in arranging for some important exchanges. We know that hundreds of advanced students of science in Europe, Asia, and elsewhere are at this moment desirous of continuing their specialized training at the educational institutions of other countries, especially America. Unfavorable monetary exchanges, high traveling costs, and the high price of living in America have made it impossible for most of these gifted students to carry through a plan that should serve science, serve their native countries, and promote international understanding.

At a recent meeting, the Executive Committee of the AAAS endorsed enthusiastically the proposal of its newly formed Subcommittee on International Relations that funds be raised to provide special international fellowships for the next two or three years, to be administered with the assistance of UNESCO and to be known as AAAS-UNESCO Fellowships.

Our Association does not have accumulated resources that can be used for such fellowships. I am authorized to appeal to the membership of the Association, and to the readers of this journal, for contributions for the establishment of the Fund. Although I would not want to discourage large contributions (in fact, many will be necessary), it will be most satisfactory if the major support of the AAAS-UNESCO Fund comes from a very

large number of Americans; a wide response would be in the democratic spirit. Small contributions are therefore in order. Please give all you can, and get some of your acquaintances, who are also sensitive to the situation confronting civilization, to give even more.

It is our expectation that in some instances the universities and colleges receiving AAAS-UNESCO Fellows will cancel tuition charges; and for some the home governments can assist with traveling expenses. But at least $2,000 should be available for each Fellow. You can count on competent operation of the fund by those who are experienced in the handling of traveling fellowships.

HARLOW SHAPLEY
President, and Chairman, International Relations Committee, AAAS

[Checks should be made out to AAAS-UNESCO Fellowship Fund and sent to 1515 Massachusetts Avenue, N.W., Washington 5, D. C.]

About People

Chalmer J. Roy, associate professor of geology, and director, Geology Summer Camp, Louisiana State University, has been appointed chairman of the Department of Geology, Iowa State College.

George Katona has been appointed associate professor of psychology at the University of Michigan, where he is directing the Federal Reserve Study for the Survey Research Center.

Jack O. Purdue, Princeton University, has been appointed instructor in chemistry and physics at Oklahoma Baptist University, and **Irma R. Fulhage,** Iowa State College, has been appointed instructor in biology.

Colleges and Universities

The Institute of Optics, University of Rochester, has developed a motion-picture camera capable of taking up to 11,000,000 frames per second. The camera, nominally rated at 5,000,000 frames per second, is believed to be more than 10 times faster than any other previous model. **Brian O'Brien,** research professor of physics and optics and director of the Institute, explained at a meeting of the Society of Motion Picture Engineers on October 21 in New York that the new camera will make hitherto impossible photographic studies quite easy to carry out, such as the investigation of electrical discharges, high explosives, shock fronts, and very rapid motion in jets and projectiles. Dr. O'Brien further pointed out that although the camera is very valuable for scientific investigations, it is not suitable for ordinary pictures, because the methods used to get the excessively high speed greatly limit the quality of the pictures. The 50-pound portable camera was developed by Dr. O'Brien and **Gordon G. Milne,** research associate in optics at the Institute.

The new 80-room laboratory which will house the Fels Research Institute for the Study of Human Development at Antioch College, Yellow Springs, Ohio, was dedicated on October 17, at which time the cornerstone was laid by Samuel S. Fels, who made the initial gift establishing the Institute 18 years ago. The new building will include laboratories for biochemical, physiological, genetic, and anthropological research, an experimental nursery school, and psychological testing rooms. The principal speaker on the occasion was Margaret Mead, associate curator of Ethnology at the Museum of Natural History, New York City.

The atmosphere of Mars, the only other planet having conditions favorable for life as we know it, has been found to contain about the same amount of carbon dioxide as does the atmosphere on earth. **Gerard P. Kuiper,** director, Yerkes and McDonald Observatories of the Universities of Chicago and Texas, has recently measured the percentage of carbon dioxide in the Martian atmosphere with his self-designed infrared spectrometer, which photographed two new carbon dioxide bands. Poisonous gases, such as methane and ammonia, are absent on Mars, according to Dr. Kuiper, but the bulk of the atmosphere may be made up of nitrogen, which does not have bands in the observable part of the spectrum. Dr. Kuiper pointed out that the Martian polar caps are probably ordinary snow and clouds, made of water. Further study with the spectrometer will be made of the polar cap on February 17, when Mars is at opposition and near aphelion, its distance from the earth then being about 61,000,000 miles, and its distance from the sun being about 154,633,000 miles. If the polar cap at that time appears large enough for spectral observation, it will at last be possible to measure the amount of water present. The absence of oceans has already indicated that the total quantity of water on the planet must be small, and the lack of water seems further confirmed to some astronomers, such as Lowell, who believe the "canals" to be strips of vegetation cultivated along the sides of artificial lines of irrigation which have been built by intelligent beings in order to make the best use of the limited water supply. Dr. Kuiper also expects to study these dark areas on Mars for the possibility of such vegetation.

The infrared spectrometer, 1,000 times more powerful than any previous instrument, the electrical parts of which were constructed by **R. J. Cushmand** and **Wallace Wilson,** physicists at Northwestern University, was first attached to the 82-inch reflector at McDonald Observatory in December 1946 and has been in constant operation ever since. It has already discovered 7 enormously strong absorption bands due to carbon dioxide near 1.6 and 2.1 μ in the Venus spectrum and has also recorded the spectra of Mercury, Saturn, and many stars.

The University of Wisconsin has introduced into its curriculum a number of history of science courses, intended to give the average college graduate, and those in the fields of pharmacy and medicine, an understanding of the position of science in contemporary society. Toward this end, four men have been appointed to new professorships in this field. **Marshall Clagett,** formerly of Columbia University, and **Robert C. Stauffer,** who also conducts a seminar in Darwinism, are teaching the history of science. **George Urdang,** professor, School of Pharmacy at Wisconsin, and director, American Institute of the History of Pharmacy, will teach the history of pharmacy, and **Erwin H. Ackernecht,** formerly assistant curator of Anthropology, American Museum of Natural History, will be professor of the history of medicine.

Meetings

The American Society for the Study of Arteriosclerosis will hold its second meeting on November 2–3 at the Hotel Knickerbocker, Chicago. The program has been divided into four sessions dealing, respectively, with Anatomic, Physiologic, Metabolic, and Therapeutic Considerations in the Study of Arteriosclerosis. Each session will be concluded with a round table, general discussion, and summary by the session chairman.

International Biometric Society Formed at Woods Hole Conference

A new international organization, the Biometric Society, was formed at the first International Biometric Conference held at the Marine Biological Laboratory at Woods Hole, Massachusetts, on September 5–6. The Woods Hole conference was attended by 100 biologists, statisticians, and other mathematicians from the United States and abroad. The Biometric Society will be concerned with the advancement of quantitative biological science through the development of quantitative theories and the application, development, and dissemination of effective mathematical and statistical techniques. Its officers are R. A. Fisher, Cambridge University, president; J. W. Hopkins, National Research Council (Ottawa), treasurer; and C. I. Bliss, Connecticut Agricultural Experiment Station, secretary. As of September 6 the other members of the Council are: Maurice Belz, University of Melbourne; R. C. Bose, Calcutta University; Detlev W. Bronk, National Research Council (Washington); Gertrude M. Cox, University of North Carolina; Carlos Dieulefait, National University of the Litoral (Rosario, Argentina); J. B. S. Haldane, University of London; A. Linder, University of Geneva; M. G. Neurdenburg, Municipal Medical and Public Health Service (Amsterdam); G. Rasch, State Serum Institute (Copenhagen); Georges Teissier, Centre National de la Recherche Scientifique (Paris); J. W. Tukey, Princeton University; and E. B. Wilson, Harvard University. Additional Council members will be announced later.

A draft constitution for the new Society was drawn up by a committee of 12 representing 10 different countries. After considering possible forms of international cooperation in biometrics, the committee decided in favor of an individual membership society without national quotas. Following a short address on international cooperation in science by Dr. Bronk at the Saturday morning session, the committee's recommendation and the draft constitution were presented to the Conference with Dr. Dieulefait as chairman. The Conference adopted the recommendation and under the chairmanship of Prof. Belz debated the draft constitution article by article. It then voted to form the Biometric Society as an international organization devoted to the mathematical and statistical aspects of biology with those present, or invited and unable to attend, as charter members. The committee which drafted the constitution was elected as the first Council with power to add others to its membership.

The Conference opened with a welcome to the Marine Biological Laboratory by Charles L. Packard, director. The Conference elected Profs. Teissier, Fisher, and Bliss as chairman, co-chairman, and secretary, respectively. Following the business session, A. F. Blakeslee, of Smith College, took the chair for a session on quantitative genetics. The principal paper, on "A Quantitative Theory of Genetic Recombination," was by Prof. Fisher with discussion opened by D. G. Catcheside, also of Cambridge University. The Friday afternoon session, under the chairmanship of Prof. Wilson, consisted of reports on recent biometric developments overseas by Drs. Rasch, Bose, and others. The scientific part of the Conference was concluded on Saturday afternoon under the chairmanship of L. F. Nims, of the Brookhaven Laboratories, with an address by Dr. Teissier on "La Relation D'Allometrie, sa Signification Statistique et sa Logique." A summary was translated by J. Monod, of the Institut Pasteur, Paris, who opened the discussion.

The proceedings of the Woods Hole conference will be published in the December issue of *Biometrics*, a copy of which will be mailed to each charter member who is not receiving the journal through membership in the Biometrics Section of the American Statistical Association.

The Biometric Society welcomes to membership biologists, mathematicians, statisticians, and others interested in its objectives. By later action of the Council charter membership is extended to all who join the Society before February 1, 1948. Further information can be obtained from the secretary, C. I. Bliss, Box 1106, New Haven 4, Connecticut, U. S. A.

Elections

At the 93rd convention of the American Pharmaceutical Association, held in the 95th year of its history at Hotel Schroeder, Milwaukee, Wisconsin, August 24–30, with more than 1,200 persons present, the following officers were elected by the House of Delegates, legislative body of the Association: Gustavus A. Pfeiffer, director, William R. Warner & Company, honorary president; Hugo H. Schaefer, Brooklyn, New York, treasurer; and Robert P. Fischelis, Washington, D. C., secretary. Other officers elected by mail ballot of the membership were Sylvester H. Dretzka, of Milwaukee, incoming president; Augustus J. Affleck, Sacramento, California, first vice-president; and Roy L. Sanford, Enid, Oklahoma, second vice-president.

Tau Beta Pi, national engineering honorary society, held its 42nd convention at the Hotel New Yorker, New York City, October 9–11. Undergraduate delegates from 76 U. S. engineering schools attended the meeting. On the evening of October 9, 7 outstanding students at Stevens Institute of Technology and the following 10 engineers from the New York area were initiated into the society: Robert M. Burns, Bell Telephone Laboratories; Stanley Bracken, Western Electric Company; Edmund A. Prentis, Spencer, White and Prentis, Inc.; Harold S. Osborne and Keith S. McHugh, both of the American Telephone & Telegraph Company; John W. Marden, Westinghouse Electric Corporation; Carl Whitmore, New York Telephone Company; Hudson R. Searing, Consolidated Edison Company of New York; Robert M. Gates, Air Preheater Corporation; and Charles E. Wilson, General Electric Company.

The society, which was founded at Lehigh University in 1885, now has 79 undergraduate chapters in engineering schools, 26 alumnus chapters, and over 48,400 members. The new officers (as of December 1947) are: Merton M. Cory, president; E. R. Moore, vice-president; and Harvey M. Merker, R. H. McCarroll, and Lawrence W. Lentz, councilors.

Recent Deaths

William M. Sylvis, 65, professor of surgery, Hahnemann Hospital, and formerly professor of anatomy, Hahnemann Medical College, Philadelphia, died October 1 at his home in Philadelphia.

Clarence H. Smith, 72, consulting otolaryngologist, Morisania City Hospital, and consulting otologist, Manhattan Eye and Ear Hospital, died October 6 at his home in the Bronx.

William D. Ennis, 70, professor emeritus of economics of engineering,

Stevens Institute of Technology, Hoboken, New Jersey, died October 14 of a heart ailment at Good Samaritan Hospital, Suffern, New York.

Francis C. Krauskopf, 69, professor of chemistry, University of Wisconsin, and a member of Wisconsin's Department of Chemistry since 1903, died of a heart attack October 16 at his home in Madison.

Francis Ernest Lloyd, 79, professor emeritus of botany and retired chairman, Department of Botany, McGill University, died October 17 in Carmel, California.

George H. Peters, 84, astronomical photographer, U. S. Naval Observatory, Washington, D. C., died in Washington October 18. Mr. Peters was known for his photographs of the solar corona, of sunspots, and of minor planets.

Sir Albert Howard, 73, agricultural scientist, former director of the Institute of Plant Industry, Indore, and agricultural adviser to states in Central India and Rajputana, died October 20 at his home in London.

Herbert Raymond Moody, 77, professor emeritus of chemistry and director of the Chemistry Laboratories, College of the City of New York, from 1905 until his retirement in 1938, died October 20 at his home in Vienna, Virginia.

The wing beat of the common drone fly may now be witnessed at a special exhibit at the American Museum of Natural History, sponsored by the Museum and the Sperry Gyroscope Company. Development of the animated enlarged scale model culminates a three-year research project during which it was necessary to use high-speed movie cameras in order to photograph the fly's wing beating 300 times per second. **C. H. Curran,** Museum entomologist and supervisor of the joint research project, pointed out that aircraft designers have been seeking the answers to the aerodynamics of insect flight, believing that the principles involved might be of practical use. In the study it was discovered that the halteres of the fly have a true gyroscopic action, but that they are not gyroscopes. A gyroscope produces balance by rotating, while the halteres produce balance by vibrating from side to side in an arc of 90°. They move opposite to the wings, moving downward when the wings rise and upward when the wings go down. **Chris E. Olsen,** Museum artist and preparator, constructed the model.

An Eye Laboratory has been established at St. Vincent's Hospital, Los Angeles, by the Estelle Doheny Eye Foundation to provide certain modern ophthalmic facilities badly needed in southern California. The Laboratory will serve as a pathological laboratory for the diagnosis and registration of pathological specimens, the preparation of slides, and the building up of a museum of eye pathology, and as a bacteriological laboratory where diagnostic scrapings, smears, and cultures may be studied, animal inoculations made, and the sensitivity of organisms to various drugs and antibiotics determined. The Laboratory will also provide facilities for fundus, gross, and slitlamp photography, maintain a library of photographs and motion pictures for teaching ophthalmology, provide an eye bank for southern California, distribute and loan certain drugs and equipment not otherwise available, and make available special equipment for radiation therapy of the eye for use outside the laboratory. The advisory board will consist of Alan Woods, Johns Hopkins Medical School; Cecil O'Brien, University of Iowa; and Phillips Thygeson, University of California. A. Ray Irvine, University of Southern California, is chairman of the original board, and Peter Soudakoff, Peking Union Medical College, will serve as full-time pathologist at the Laboratory. The Foundation and Laboratory are made possible by the donation of Mrs. Edward Laurence Doheny.

The Atomic Energy Commission has recently appointed as the director of its Office of Public and Technical Information **Morse Salisbury,** formerly director of information, U. S. Department of Agriculture, and currently assistant secretary-general, International Emergency Food Council. The associate director will be **Edward R. Trapnell,** formerly public relations adviser to Major Gen. Groves, Commanding General, Manhattan District, and acting director of information, AEC; the chief of declassification, **Harold Fidler,** formerly assistant director of research, Oak Ridge; and the chief of technical information, **Alberto Thompson,** formerly director of the publication of technical information, Atomic Energy Project. The responsibility of the Office of Public and Technical Information is to screen all material to be issued to the public concerning the Commission's activities and ascertain that all has been properly declassified and cleared with respect to restricted data as defined in the Atomic Energy Act. This work of declassification is being carried on by a consulting staff of over 100 scientists throughout the project. The "Declassification Guide" developed by the Manhattan District in accordance with recommendations of a committee headed by Richard C. Tolman, California Institute of Technology, sets forth the standards of the declassification process of the Office.

The U. S. Office of Education has reported that American colleges and universities need to almost double their existing classroom facilities. They now need an additional 90,000,000 square feet of classroom space and will need a total of 300,000,000 square feet by 1950. The Veteran's Educational Facilities Program Section of the Office of Education pointed out that this is a construction job comparable to building an entire business district for a large city. This fall's college enrollment has been estimated to be 2,750,000 students, 600,000 more than last fall. It has also been estimated that in 1951–1952, the enrollment will drop to 2,477,000, rising again to 2,924,000 in 1959–1960.

The General Disposals Division, Office of the Foreign Liquidation Commissioner, 4th and Jefferson Drive S.W., Washington 25, D. C., is offering portions of two German chemical plants for sale to U. S. industry. These are the Dynamit A. G. Geestacht-Krummel plant, on the Elbe River about 19 miles southeast of Hamburg, its equipment consisting of 21 items used in the production of plastics with grinding mills, distilling vats, especially lined storage tanks, a crusher for artificial resins, and allied facilities; and the Paraxol at Lippoldsberg, including one producing unit for formaldehyde and two units for the production of pentarythritol. Also available to U. S. purchasers is the electrical generating equipment used with these units. Inventories of these plants and information concerning inspection and bids may be obtained from the General Disposals Division. December 10 is the closing date for sealed bids on both plants.

COMMENTS

by Readers

One wishes that every scientist and engineer might read the memorandum which accompanied President Truman's veto of the recent National Science Bill, S.526, and the more recent pamphlet, *Science and public policy*, by John R. Steelman, chairman of the President's Scientific Research Board.

From the first comes an appreciation of the complications that necessarily inhere in attempting, as in S.1850 and again in S.526, to make a single organization responsible at once for the allocation of funds to support pure science and for the direction of military research.

The latter makes it abundantly clear that in the rapid growth of science the politician sees ample justification for giving it his increasingly close attention so that it may be properly assimilated into the national life. Repeatedly the report stresses the concept of planning and guiding research effort so as to coordinate it more closely with the scientific programs of the Federal bureaus and with military research as well as with the industrial needs of the Nation (see, e.g., passages on pp. 5, 6, 9, 26, 31, 34, and 61).

Thus, the combined effect of the veto memorandum and the Steelman report is most revealing.

Doubtless, the President stands on firm ground when he demands executive control of any government agency engaged in military research and development. This alone would have justified his veto, but he implies very pointedly that he vetoed S.526 because it failed to give him the broad control over scientific effort which he believes he should have. This is the minimum political price which must be paid if the foundation is created to discharge the dual purpose.

So why strive longer to domicile an antelope and a bear in the same pen? Why create the national fiction that the interests of pure science require intimate association with military research, or vice versa? I wish to imply nothing for or against the hypothecated need of a central organization for military research and development after the pattern of OSRD. This may be very desirable; but in proportion as it is desirable, it is certainly undesirable that it be yoked to the most international of all undertakings. To do this seems as confusing an approach to world relationships, scientific and otherwise, as it is an unpromising approach to the problem of supporting science here at home.

Given a clean-cut separation of these two functions that envisages a science foundation whose sole purpose is to allot funds for pure science, this foundation could receive Federal aid though it were quite unattached to the executive arm of the Government. Congress can and does continually appropriate money to organizations over which the President has no control.

Adopting such an arrangement for science, the resulting foundation might have a wholly private status, or it might be quasi-governmental after the pattern of the National Academy of Sciences. Some will recall that the Willis Bill before the 79th Congress proposed this latter arrangement. Its sponsors recognized the basic undesirability of associating military research with the allocation of considerable sums for the support of pure science, and feared also the additional threats to scientific freedom which must lie in any foundation subservient to the executive arm of the Government. But what in the minds of some of us is equally important, an extra-governmental agency closes no door upon whatever personal and corporation giving may again be stimulated, either by modification of income tax credits or otherwise.

We do not, however, regard the road leading to such an agency as strewn with violets. American science is to date inexperienced in the centralized partitioning and distribution of its lifeblood. The veto memorandum, in effect, declares that the problem cannot be solved without the intervention of political personnle and political authority; and though this is, perhaps, its one unhappy note, all must admit that the President's apprehension offers a constructive warning. He points out that members of the foundation, as envisaged in S.526, would be employees of institutions or organizations eligible for grants, and that out of the resulting conflict of interests and responsibilities, and regardless of their complete integrity, the members might be suspected of favoritism. But the course he proposes of taking control away from the scientific members and giving it to political appointees will be regarded by many as epitomizing the dangers most to be feared. Fortunately, alternatives are at hand.

There is, for example, the representative type of institution, operated within the compass of science itself. After all, broad representation is the traditional American way and protects to a degree which is probably unattainable otherwise.

This solution might be approached through a sort of constitutional convention, whose deliberations so far as American science is concerned would promise to rank in significance with those epochal sessions held in Philadelphia a century and a half ago. The aim of this science convention would be to formulate and agree upon a representative central fiscal agency. This would be embodied in a constitution and a system of elections for officers and members such as to merit the approval of both the scientific fraternity and leaders of public opinion. As to the desired safeguards and flexibility of such an agency, these have been emphasized so often in the course of the debates on science legislation that they need only be summarized in a word or two here. Chiefly, they would insure that the allocations of research money would be widespread geographically, they would insure the recognition of scientific merit and promise wherever these might arise, and they would shoulder few, if any, encumbrances upon the recipient. (ROBERT W. KING, *463 West Street, New York City.*)

The present communication deals with almost forgotten material on the dental aspects of prenatal injury. Preparation of a bibliography on the effects of German measles during pregnancy recalled to the writers a concept, commonly taught in dental schools in this country, to the effect that acute infectious diseases in the mother during pregnancy will cause congenital anomalies of

the deciduous dentition in the infant, if these diseases occur during the time when the teeth are forming. It is also understood that these same diseases in infants and young children, occurring during the period when the permanent teeth are forming, will similarly affect these teeth.

A partial study of the available dental literature on this subject has revealed an interesting discussion which includes the presentation of a case similar to those found by Evans (*Med. J. Aust.*, 1944, **2**, 225). This was reported in 1893 by J. J. R. Patrick as follows (*Dent. Rev.*, 1893, **7**, 439):

"I have entered thus far into a description of the origin and development of the teeth, in order to illustrate the detrimental influence of eruptive fever on the teeth during the periods of their formation; and while eruptive fevers are not the only factors to be recognized in producing abnormal conditions in tooth development, I consider such fevers a prolific source of faulty nutrition in these organs, as the following cases observed in my practice will fully exemplify.

"Mrs. S., during the fifth month of gestation was afflicted with scarlet fever—recovering, in the course of time gave birth to a child. This child's teeth appeared unusually early, the enamel discolored, pitted and granular and absent at the incisive margins, and the teeth barely extended beyond the gum. He is now fifteen years old with all his permanent teeth except the third molars. These second teeth, with the exception of a little decay, are in good condition, the enamel smooth and white and all the teeth large and strong.

"Three years later another child was born, and soon afterward the first child contracted the measles and the second child also contracted the disease. In the course of time the deciduous teeth of the second child appeared, all in excellent condition, but were lost unusually early, and the second set appeared in the following order: The sixth year molars at four years. The central incisor at five years. The premolars between the sixth and seventh years; and the cuspids between the eighth and ninth years. All these teeth are discolored, pitted and granular, and the enamel is worthless as a protection to the dentine."

Later in the same year Dr. Patrick attended the World's Columbian Dental Congress at Chicago, where a paper on the pathology of congenital defects of the deciduous dentition was presented by Otto Zsigmondy. During the discussion of this paper Dr. Patrick made the following remark (*Trans. World's Columbian dent. Congr.*, 1894, **1**, 65):

"All eruptive diseases during gestation must necessarily affect the enamel of the deciduous teeth if these eruptive diseases take place during the formative process of the enamel. How could it be otherwise?"

The quotations given above not only show that Dr. Patrick had developed a clear concept of the role of acute disease of the mother in the causation of congenital defects of the infant in the field of dental development, but also point out two factors which are of importance in the current efforts to clarify the medical aspects of this problem. The teeth are relatively permanent structures, and their embryology has been worked out in considerable detail. It is therefore apparent that the presence or absence of defects in the deciduous teeth will be of great importance in the evaluation of the effects of various disturbances of pregnancy on the fetus during the period of tooth formation. A study of the simultaneous occurrence of dental defects and malformations in other organs will also be of considerable interest.

Dr. Patrick's second case points out that the problem of developmental anomalies is not limited to the period of gestation, but also extends for some time beyond the birth of the child. This postnatal aspect of the problem deserves more study from a medical point of view. The importance of the presence or absence of dental defects, especially in conjunction with defects in other parts of the body, is again apparent. (R. J. M. HORTON, *Harvard School of Public Health*, and J. M. DUNNING, *Harvard School of Dental Medicine*.)

To express in a mathematical formula a complicated physiological response such as that involved in body-temperature reactions of cattle to climate, the fundamental requirement is that it be based on as complete an accumulation of facts as possible. To modify a formula that satisfies this condition by introducing a factor based on an assumption unsupported by experimental evidence is to confuse rather than to advance the knowledge of the subject.

In a recent paper R. F. Gaalaas (*J. dairy Sci.*, 1947, **30**, 79–85) has modified the formula

$$HT = 100 - [10(BT - 101.0)]$$

originated by Rhoad (*J. animal Sci.*, 1942, **1**, 85) to

$$HT = 100 - [14(BT - 101.0)].$$

In the Rhoad formula the factor 10 is used merely to remove the decimal from the result within the parentheses. In this manner a whole-number coefficient in a scale of 100 is obtained, with 100 equal to perfect efficiency in maintaining a normal body temperature of 101.0°F., under prescribed rules of a test procedure (A. G. Rhoad. *Trop. Agric.*, 1944, **21**, 162-164).

The factor 10 was changed by Gaalaas (p. 80) "based on the assumption that a body temperature of 108°+ at 90°F. air temperature and under otherwise normal conditions would indicate a complete loss of control in the regulation of body temperature, or zero per cent efficiency in eliminating surplus body heat. Conversely, a body temperature of 101°F. is considered normal and a cow that would maintain that body temperature at 90°F. air temperature would be considered 100 per cent efficient. . . ."

The reader is led to believe that the factor 14 was derived by dividing the 7° range between 101 and 108 into 100 equal parts, thereby placing a value of 0.14285716 . . . ∞ on each tenth of a degree on the clinical thermometer.

In correspondence, Gaalaas states that the factor 14 is a correction factor necessary because his cows had "access to shade instead of requiring them to be held in the sun. . . . The factor 14 is enough larger to correct for the observed average difference in body temperatures." A check on the results published earlier by Gaalaas (*J. dairy Sci.*, 1945, **28**, 555-563) gives credence to this interpretation of the origin of the factor 14 and is acceptable as a correction factor, as it is properly supported by satisfactory data.

One wonders, therefore, why an unsupported assumption is given as the base for changing the factor 10 to 14 in the original formula! (ALBERT O. RHOAD, *Inter-American Institute of Agricultural Sciences, Turrialba, Costa Rica.*)

TECHNICAL PAPERS

Chloromycetin, a New Antibiotic From a Soil Actinomycete

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From a soil sample collected in a mulched field near Caracas, Venezuela, a *Streptomyces* sp. was isolated.[1] Agar streak cultures were found to inhibit adjacent inocula of *Bacillus mycoides*,[1] *B. subtilis*,[1] *Mycobacterium tuberculosis* var. *hominis* (ATCC 607[1] and H37Rv[2]), *Staphylococcus aureus*,[1,3] *Streptococcus pyogenes*,[3] *Brucella abortus*,[3] *Escherichia coli*,[1,3] *Klebsiella pneumoniae*,[3] *Salmonella schottmuelleri*,[3] and *Shigella paradysenteriae* (Sonne).[3] When the organism was grown in liquid media in shaken flasks, filtrates of these submerged aerated cultures proved to possess marked antibacterial activity in broth-dilution assays against several gram-negative bacteria, notably *S. paradysenteriae* (Sonne), and indications of antirickettsial activity. From these filtrates a crystalline antibiotic has been isolated, for which the name Chloromycetin is proposed.

TABLE 1

Vol. medium	Container (capacity)	Yield (μg./ml.)
100 ml.	Erlenmeyer flask (500 ml.)	55
18 l.	Glass fermenter (30 l.)	85
100 gal.	Rotary aluminum drum (200 gal.)	49

The organism has been found to produce Chloromycetin in aerated submerged culture in various media. A satisfactory formula is: maltose, 1.0 per cent; casamino acids (Bacto), 0.5 per cent; distillers' solubles, 0.5 per cent; and sodium chloride, 0.5 per cent. Typical yields with this medium in various containers are given in Table 1. Potency is estimated turbidimetrically in terms of weight of crystalline material from a standard curve for 50 per cent inhibition of *S. paradysenteriae* (Sonne).

It was found that Chloromycetin could be concentrated and purified by extracting acidified culture filtrates with ethyl acetate, removing the solvent by distillation *in vacuo*, extracting the antibiotic with diethyl ether, chromatographing the ether solution over aluminum oxide, removing the solvent by evaporation, extracting the residue with water, extracting the aqueous solution with petroleum ether, and concentrating the aqueous solution. During the course of the concentration the antibiotic crystallized. After three recrystallizations from methylene dichloride, ethylene dichloride, and a mixture of diethyl ether and petroleum ether, colorless needles or elongated plates having the following properties were obtained: m.p., 149.7–150.7°C. (corrected); $(\alpha)_D^{25}$, − 25.5° (ethyl acetate)[4]; solubility in water at 25°C., about 2.5 mg./ml.; very soluble in methanol, ethanol, butanol, propylene glycol, and acetone; analysis: C, 41.11; H, 3.89; N, 8.60; Cl (nonionic), 21.71.[5]

Chloromycetin is a neutral compound and is unique in that it contains both nitrogen and nonionic chlorine. It is furthermore characterized by being stable at room temperature in aqueous solutions over the pH range of 2–9 for more than 24 hours, and in distilled water is unaffected by boiling for 5 hours.

The *in vitro* activity of the crystalline material against several bacteria is shown in Table 2. The test against *Br. abortus* was performed by dissolving varying amounts of the crystals in agar and streaking with *Br. abortus*.[3] *Myco. tuberculosis* was assayed by an end-point broth-dilution method.[2] The other organisms were tested by a turbidimetric method.[3]

TABLE 2

WEIGHT OF CRYSTALLINE CHLOROMYCETIN CAUSING INHIBITION OF TEST ORGANISM

Species	μg./ml.	Inhibition (%)
Brucella abortus	2.0	100
Escherichia coli	0.33	50
Klebsiella pneumoniae	0.33	50
Mycobacterium tuberculosis (H37Rv)	12.5	100
Proteus sp.	0.33	50
Salmonella schottmuelleri	0.33	50
Shigella paradysenteriae (Sonne)	0.2	50
Staphylococcus aureus	1.0	50

The crystalline material showed marked chemotherapeutic activity against *Rickettsia prowazeki* in screening tests using chick embryos[6] and against a number of rickettsiae and one virus when tested in embryonated eggs or in mice (*1*).

The intravenous LD_{50} for 20-gram mice is 3.0 mg./mouse. In contrast to streptomycin, Chloromycetin appears to be well absorbed when administered orally to mice and dogs.[7]

Detailed accounts of these studies are in preparation.

Reference

1. SMADEL, J. E., and JACKSON, E. B. *Science*, 1947, **106**, 418.

[1] In Paul R. Burkholder's laboratory, Yale University.
[2] In Guy P. Youmans' laboratory, Northwestern University.
[3] In the Research Laboratories, Parke, Davis & Company.
[4] Determined by Robert L. Harris, Parke, Davis & Company.
[5] Determined by A. W. Spang, Parke, Davis & Company.
[6] Determined by I. W. McLean, Jr., Parke, Davis & Company.
[7] Determined by O. M. Gruhzit, Parke, Davis & Company.

Chloromycetin, an Antibiotic With Chemotherapeutic Activity in Experimental Rickettsial and Viral Infections

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A new antibiotic, Chloromycetin (*1*), has been found to have a remarkable chemotherapeutic effect on a number of rickettsial agents and on one of the viruses. This substance was prepared in the Research Laboratories of Parke, Davis & Company and submitted to this Department as highly purified crystalline material; preliminary tests (*1*) had indicated that Chloromycetin possessed activity against *Rickettsia prowazeki*.

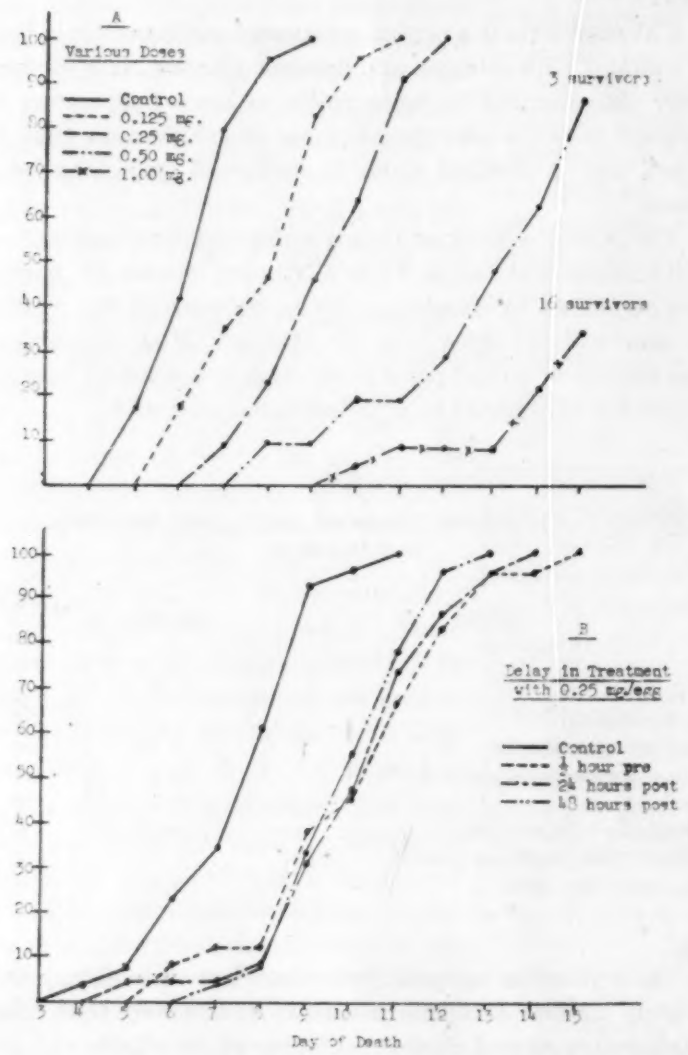

Fig. 1. Rickettsiostatic effect of drug in embryonated eggs infected with *R. orientalis*.

Initial tests were performed using groups of 24 seven-day embryonated eggs which were infected by the yolk sac route with the Gilliam strain of *R. orientalis* and treated by the same route with varying amounts of drug given at different times. Eggs were examined daily and the time of death of embryos noted. Data are summarized in Fig. 1 as the percentage mortality in the various groups on different days after infection. The experiment summarized in A, Fig. 1, shows the effect of varying amounts of drug given in a single injection ½ hour prior to infection. It is evident that the smallest dose used, namely, 0.125 mg./egg, resulted in a definite prolongation of life of the embryos. The beneficial effect increased step by step as the dose was increased. All of the embryos in the group receiving 1.0 mg. were alive when the last of the control eggs died. Furthermore, 16 of the 24 embryos were still alive in this group on the 15th day after infection, when the experiment was terminated since hatching was to be expected. Eight chicks did hatch from this group of 16 survivors. Section B of Fig. 1 summarizes an experiment in which 0.25 mg. doses of drug were given to each of 24 eggs in three different groups; one group was treated ½ hour prior to infection, another 24 hours, and a third 48 hours, after infection. It is apparent that all embryos were equally benefited by the treatment; the average prolongation of life in each of the groups was in the neighborhood of 2½ days.

The chemotherapeutic effect observed in treated mice infected with scrub typhus was as satisfactory as that obtained in experiments with embryonated eggs. Table 1 summarizes the results of studies on mice infected by the intraperitoneal route with 25–100 m.l.d. of the Karp strain of *R. orientalis*.

TABLE 1

Chemotherapeutic Effect Obtained in Mice Infected With *R. orientalis*

Experiment	Treatment			Dilution of infectious inoculum		
	Mg./day/mouse	Route	Day begun in relation to infection	10^{-5}	10^{-6}	10^{-7}
1	Controls	Injected intraperitoneally		8/8	8/8	2/7
	2.5		1 post	0/8		
	1.5		1 "	0/8		
	0.75		1 "	2/8		
	0.5		1 "	5/8		
	0.25		1 "	5/8		
	0.10		1 "	3/8		
	5.0	Fed in water	1 pre	0/8		
	5.0		2 post	1/8		
	3.0		1 pre	0/7		
	1.5		1 "	1/8		
2	Controls	Injected intraperitoneally		7/8	7/8	3/8
	2.5		1 post	0/8		
	2.5		5 "	0/8		
	2.5		8 "	1/8		
	2.5		10 "	3/8		
	0.75		1 "	2/8		
	0.75		5 "	2/8		
	0.75		8 "	6/8		
	0.75		10 "	7/8		

Animals were treated either by a single daily intraperitoneal injection or by oral administration of the designated amount of drug; in the latter instance it was dissolved in the drinking water. Animals were given their first injection 18 hours after infection or at a later date designated in the table. Mice which were fed the drug generally were started on it the day before inoculation of infectious material. In all instances mice were treated from the designated time through the 20th day after infection. The data indicate that a single daily intraperitoneal dose of 1.5 mg. of the drug protected all of the mice. Half this amount protected the majority, while doses as small as 0.1 mg./mouse had some chemotherapeutic effect. All of the mice which received 3.0 mg. of the drug by mouth per day sur-

vived, as did practically all of those receiving half this amount. It is to be noted that oral administration of 5.0 mg./day begun two days after infection protected 7 of the 8 mice from death. The fact that an excellent chemotherapeutic effect can be obtained even when administration of the drug is delayed for 10 days after infection is indicated by the results of the second experiment (Table 1). Seven of the 8 untreated control mice which received the 10^{-5} dilution of infectious material died between the 14th and 18th day. In contrast, only 3 of 8 mice succumbed in the group which received 2.5 mg. of the drug beginning on the 10th day after inoculation; these died between the 15th and 20th days. The majority of the mice which received 0.75 mg. daily were protected when the drug treatment was begun as late as 5 days after infection but not when it was begun 8 days afterward.

Results essentially identical with those just described have been obtained in embryonated eggs and mice infected with the agent of rickettsialpox (*R. akari*). Furthermore, the results of experiments in which embryonated eggs were infected with *R. prowazeki*, *R. mooseri*, *Dermacentroxenus rickettsi*, or the 6-BC or P-4 strains of psittacosis duplicated almost exactly those summarized in Fig. 1. A good chemotherapeutic effect was demonstrable in mice infected with the 6-BC strain. The antibiotic has been ineffective in the treatment of mice infected with Japanese encephalitis virus and in eggs infected with variola virus and influenza A virus.

Inasmuch as control mice and embryonated eggs which received amounts of the drug comparable to the maxima used in the above tests remained unaffected, Chloromycetin appears to be of low toxicity. Its low toxicity, its absorption from the alimentary tract, and its beneficial effect when given relatively late in disease suggest that it may be valuable in the treatment of patients.

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Initiation of the Cone Gall of Witch Hazel

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The control of growth and differentiation leading to the orderly development of the plant and animal body continues to be the central problem of biology. From Darwin and Herbert Spencer to the present time, theories of heredity have demanded some sort of controlling substance, whether envisaged as a physiological unit, a gemmule, a gene, or even as a hierarchy of biophores, determinants, and ids. In theories of the last 50 years the location of these units has been placed in the chromatin of the nucleus, and only recently have these specific, controlling, and self-propagating entities been ascribed to a location in the cytoplasm, the "plasmagenes" of Wright (*1*). A substance initiating, stimulating, and directing development and differentiation has been found in the cells of the cone gall of witch hazel (*Hamamelis virginica* L.). It is injected into the young leaf by "stings" of an aphid (*Hormaphis hamamelidis* Fitch) which feeds on the neoplasm induced by its presence.

The process of stinging is quite different from that of feeding. When stinging, the stem mother inserts her stylets into and between the cells of the young leaf and injects minute drops of a substance secreted by glands opening into the stylar canal. The sting substance cannot be confused with the salivary secretion because it shows characteristic staining reactions and properties of refraction.

Cells receiving the injected sting material dedifferentiate, undergo rapid mitotic divisions, and redifferentiate, not into cells of the normal witch-hazel leaf tissues, but into cells of other and different tissues which organize the gall. The cells show the effects of the stings immediately, and when about 150 stings have been made over a small circular area of the leaf, the cells of this area first become etiolated and then, by growth in size and number and by tissue differentiation produce the highly specialized cone gall. This is not a haphazard excrescence on the leaf, but in symmetry and harmonious unity of cells and tissues shows the same phenomena of functional adaptation that are familiar in the individual. It differs from an individual in its inability to reproduce.

The injected material, when stained with acid fuchsin and jod green consists of a blue ground substance in which minute crystalloids are embedded. The material of the crystalloids seems to pass readily from cell to cell, especially from phloem parenchyma to adjoining cells. The crystalloid is a tiny, refractory, deeply staining body characterized by its faceted appearance and showing a reddish or purplish cast in such stains as gentian violet, hematoxylin, safranine, congo red, acid fuchsin, basic fuchsin, Feulgen, and pyronine.

The behavior of the injected material is somewhat different when injected directly into the cytoplasm and when injected into intercellular spaces. When injected directly, it is seen first in the cytoplasm as a single globule containing, usually, one refractory crystalloid. The globule enters the nucleus and then the nucleolus, where the crystalloid breaks up into smaller bodies.

When the injection is intercellular, the globule is usually much larger and at first does not show crystalloids, though a small body showing the same staining reactions may be present. Crystalloids form within the globule which enters the leaf cells, occasionally the inner epidermal and spongy parenchyma cells, but much more often the phloem parenchyma. From the phloem parenchyma the sting material passes into palisade or even into cells of the upper epidermis. During its existence in the cytoplasm of the phloem parenchyma it may break up into smaller globules, each with its crystalloid or may lose its crystalloids singly into the cytoplasm. Whether injection is intra- or intercellular, the end result is the entry of the crystalloids into the nucleolus. There they may fuse to form a larger, single crystalloid which breaks up into smaller ones when the nucleus enters prophase.

As mitosis approaches, the bodies become more numerous, and are distributed to the daughter nuclei, where they are found in the nucleolus as they were in the mother nucleus. They appear not to be capable of self-propagation. For gall formation to continue normally, additional sting material must be injected repeatedly into the leaf. During the entire growth of the gall the stem mother continues to sting in intervals of feeding. Only the stem mother can initiate gall

formation; no other generation in the life history of the aphid possesses this power. If the stem mother dies or is removed from a developing gall, growth of the gall soon ceases. Tissues differentiated in the gall do not revert to normal leaf tissues.

The gall may be looked upon as a neoplasm. Further studies are planned on the chemistry of the substance causing it to form. A detailed report of observations here summarized is in preparation.

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A Relationship Between Cystine and Pyridoxal or Pyridoxamine in the Nutrition of Certain Bacteria

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Cystine has been found to be essential for the growth of *Lactobacillus arabinosus* (*5*) and *L. casei* (*3*), although in a more complete synthetic medium it was reported to be unessential for *L. arabinosus* (*2*).

In experiments designed to assay cystine by *L. arabinosus* 17-5, using the medium of Stokes, *et al.* (*10*), near maximum growth occurred at 37° C. with no cystine added to the medium. It was subsequently found that the pyridoxamine in the medium eliminated the requirement of this organism for cystine (Table 1). Pyridoxal had the same effect, while pyridoxine had little or no effect on growth. Similar results were obtained with *Streptocccus fecalis* and *L. casei*, although cysteine was found by Dunn, *et al.* (*2*) to be essential for *L. casei* in a medium containing pyridoxal and pyridoxamine. The cystine requirement of *L. delbrückii* LD5 and *Leuconostoc mesenteroides* P-60, however, was not affected by the presence of pyridoxamine or pyridoxal, which agrees with results of Dunn, *et al.* (*2*). Similar effects of these compounds on certain other amino acid requirements of various lactic acid bacteria have been reported by Stokes and Gunness (*9*) and Lyman, *et al.* (*4*).

TABLE 1

Interchangeability of Cystine With Pyridoxal or Pyridoxamine in the Nutrition of Certain Bacteria

(ml. 0.1 N NaOH/10 ml. culture)*

Organism	No cystine; no vitamin B_6	100 γ/ml. cystine; no vitamin B_6	100 γ/ml. cystine + 0.4 γ/ml. pyridoxamine†	No cystine; 0.4 γ/ml. pyridoxamine†	No cystine; 0.4 γ/ml. pyridoxal†	No cystine; 0.4 γ/ml. pyridoxine†
L. arabinosus 17-5 (A.T.C.C. #8014)	1.30	6.20	9.50	7.60	7.95	2.00
L. casei (A.T.C.C. #7469)	1.50	6.50	9.55	7.55	7.95	2.55
Str. fecalis (A.T.C.C. #9790)	1.50	6.60	6.70	5.75	5.90	1.70
Leuc. mesenteroides P-60 (A.T.C.C. #8042)	1.25	3.45	8.80	1.80	1.80	1.90
L. delbrückii LD_5 (A.T.C.C. #9595)	1.15	2.13	10.05	1.78	1.00	0.70

* Medium of Stokes, *et al.* (*10*), except for changes in cystine and vitamin B_6 group noted.

† Seitz-filtered; added aseptically to sterile medium.

When incubated at 30° C. instead of 37° C. with 0.4 γ/ml. of pyridoxamine but no cystine, *L. arabinosus* and *L. casei* grew slightly, while *Str. fecalis* grew almost equally as well as at 37° C. These data indicate that the mechanism whereby pyridoxamine replaces the cystine requirement of these organisms is not necessarily associated with the optimum growth temperatures of the organisms.

Since cystine is essential for *L. arabinosus*, *L. casei* and *Str. fecalis*, their growth in a medium deficient in cystine, but containing pyridoxamine or pyridoxal, indicated that cystine was synthesized from ingredients of the medium. To test this, *L. arabinosus* and *Str. fecalis* were grown 3 days at 37° C. and *L. casei* 6 days at 37° C. in the medium of Stokes, *et al.* (*10*) containing 0.4 γ of pyridoxal/ml. (Seitz filtered; added aseptically), but from which cystine was omitted. The washed cells were acid hydrolyzed and the hydrolysates assayed by *Leuc. mesenteroides* P-60. *L. arabinosus* contained 0.38 per cent, *L. casei* 0.65 per cent, and *Str. fecalis* 0.26 per cent cystine on the basis of dried cells. The cystine thus formed may originate from methionine, as shown by Tarver and Schmidt (*11*) to occur in rats fed methionine containing isotopic sulfur, and/or from serine, as reported by Stetten (*8*) to occur in rats fed serine containing isotopic nitrogen. Whatever the origin of the cystine, pyridoxal and pyridoxamine have an essential role in its synthesis in such a medium.

Some of the irregularities reported in the microbiological assay of cystine by *L. arabinosus* and *L. casei* (*1*, *6*) can probably be explained by the presence of pyridoxal or pyridoxamine in the medium or in samples assayed. Also, a medium deficient in cystine but containing 0.4 γ of pyridoxine/ml., sterilized by autoclaving at 15 pounds pressure for 13 minutes, permitted considerable growth of these cultures. This was probably a result of pyridoxamine being formed by the interaction of pyridoxine and amino acids in the medium during sterilization (*7*), and indicates another reason for irregularities in the assay of cystine by *L. casei* and *L. arabinosus*. Furthermore, since temperatures from 30° to 37° C. are used for the growth of these bacteria, the degree to which pyridoxal and pyridoxamine contained in the medium replace the requirement for the added cystine varies with the particular temperature of incubation.

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Protection of Synaptic Transmission Against Block by Nicotine

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During the past year we have studied the effects of various drugs on synaptic transmission in the crayfish; the results will be described elsewhere. In the course of this investigation many drugs were found to have no effect. In such cases a check was made on the preparation by applying a dose of nicotine (10^{-5} grams/cc.) 10 minutes after the original drug. Control tests had shown that nicotine in this concentration blocks transmission in 1–2 minutes. As expected, the presence of most drugs did not influence this action. With some, however, either the nicotine was without effect or the block was greatly delayed. Evidently under certain conditions the preparation is protected against the action of nicotine. Since this situation seems to be of considerable interest, the following preliminary report is presented at this time.

The synapse used in these investigations is between a giant fiber in the central nervous system and a motor fiber in an abdominal root of *Cambarus clarkii* (*3*). The preparation was kept in a bath containing 100 cc. of crayfish perfusion fluid, the drugs being added to this bath. The giant fiber was stimulated between the 5th and 6th abdominal ganglia, while the postganglionic response was led off the 3rd root of the 3rd ganglion. Stimuli were delivered throughout the experiment at 30/minute, at which rate, in the absence of drugs, the postganglionic response remains unchanged for several hours.

The protecting effect was first noted with two drugs, anabasine and nornicotine,[1] which are closely related in structure to nicotine. In a typical experiment, anabasine 10^{-4} was administered. After a transient facilitation, transmission returned to normal. At the end of 10 minutes, nicotine 10^{-5} was given. This had no effect. Ten minutes later, nicotine 10^{-4} was administered, but even this high concentration had no effect for at least 10 minutes.

The results of similar experiments, made with a number of other drugs, permit the following classification to be made:

(a) Drugs which in low concentration protect the crayfish synapse from the action of nicotine, but which block the synapse in higher concentration: anabasine, nornicotine.

(b) Drugs which in subthreshold doses show no protection against nicotine and which block transmission in higher concentrations: alcohol, DFP, eserine.

(c) Drugs which neither protect against nicotine nor block synaptic transmission: acetylcholine, adrenalin, atropine, coramine, picrotoxin, prostigmine, strychnine.

An unexpected result was obtained in experiments in which the nicotine was left in the bath after transmission was blocked. Complete recovery of the root potentials occurred within 40 minutes. Renewed application of nicotine in the same or even higher concentration was now without effect. The same result was obtained when the preparation was washed with fresh perfusion fluid after block by nicotine.

[1] We wish to thank R. C. Roark, Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture, Beltsville, Maryland, for supplying these drugs.

A similar effect has been observed with eserine. After block by this drug, transmission rapidly returns to normal on washing with fresh fluid. Another dose of eserine, of even higher concentration, is now without effect. The preparation is also protected against the action of nicotine.

Protection against nicotine has been reported by other workers. Novocaine antagonizes the effects of an intravenous injection of nicotine on the heart, blood pressure, and intestine of the dog (*1*). Sulfathiazole inhibits the action of nicotine in the isolated intestine (*2*). The present study, however, has the advantage of confining drug action to synaptic transmission.

Biological competition between structurally related compounds is well known (*4*). In this type of action it is generally considered that the compounds involved compete for attachment to a specific receptor. Such a mechanism is not completely adequate to explain the phenomena described in the present paper, however. Nicotine evidently has a twofold action on synaptic transmission. When first applied, it blocks transmission. As recovery occurs, this blocking action is lost, but a protecting action remains, since further doses of nicotine are without effect. This shift from a blocking to a protecting action suggests that a change takes place in the nicotine molecule by which it becomes ineffective as a blocking agent but remains attached and thereby prevents the action of fresh nicotine. The attachment must involve a firm bond, since washing with perfusion fluid does not interfere with this protection.

Anabasine and nornicotine, which have much less blocking action, seem to attach as readily as nicotine and therefore protect against it. During recovery from nicotine block, nicotine may be transformed into a compound like these or into a related compound with a pure protective action.

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Role of Inhibitors in Soybean

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It is now recognized that cooking or autoclaving increases the nutritive value of the protein of soybean. The general opinion is that cooking increases the availability of cystine and methionine. Almquist, *et al.* (*1*) and Hayward and Hafner (*8*) demonstrated that the limiting amino acid in soybean is methionine, and heating under pressure increases the availability of this amino acid. Evans and McGinnis (*4*) found that the retention of organic sulfur is increased from 34 to 52 per cent and that of methionine from 58 to 74 per cent in autoclaved soybean. But Melnick, *et al.* (*9*) found no increase in the retention of methionine in autoclaved soybean, and from their experiments they concluded that the higher biological value of autoclaved soybean was due to an increased rate of release of methionine rather than a higher degree of its availability. Ham and Sandstedt (*6*) found that a dilute acid extract of raw

[1] Our thanks are due to V. Subrahmanyan for his keen interest in the work.

soybean contained a substance which greatly reduced the activity of trypsin *in vitro*. Ham, *et al.* (*7*) found that a solution of the partially purified inhibitor produced lowering of growth in chicks fed on a well-balanced diet. In a previous communication from this laboratory (*3*) it was stated that glycinin is more nutritive than autoclaved soybean. It was believed that the enhanced nutritive value of glycinin was due to elimination of the proteolytic inhibitor, as also any toxic factor which may be present in raw soybean.

The present investigation was undertaken to see whether the presence of the inhibitor would affect the nutritive value of soybean protein digested with enzyme so that the amino acids are in free form. According to the hypothesis of Melnick, *et al.*, the biological value of the digest is expected to be higher than the raw bean, because all the amino acids, including methionine will be simultaneously available for utilization.

The digest was prepared by subjecting soybean meal to digestion by papain. Acid hydrolysis was not resorted to because it would destroy tryptophane and other possible essential peptide factors like strepogenin, as suggested by Woolley (*5*). Papain was chosen for the proteolytic digestion, since the raw soybean meal contained the tryptic inhibitor. The soybean meal was finely ground and suspended in about four times its weight of water and digested with an active preparation of papain. The digestion was carried out at 50°C. for 48 hours. A control was run, using a boiled solution of the enzyme which was maintained at the same temperature. Both samples were then dried in a current of warm air. It was found that the inhibitor was destroyed to a small extent in the course of drying. A requisite amount of the inhibitor solution extracted from raw bean was added to both the extracts in order to restore the original activity.

The biological value and the digestibility coefficient of the protein in the digested and control samples were determined by the usual nitrogen balance method. The proteins were fed at a level of 10 per cent (nitrogen × 5.7). The results are as follows:

	Average digestibility coefficient	Average biological value
Digested sample	89.6	45.9
Control sample	89.2	44.7

The nitrogen in the digested sample was analyzed, and it was found that 91.6 per cent of the total nitrogen of the meal was in the nonprotein form, as estimated by its solubility in 7 per cent trichloroacetic acid, and 90 per cent of the total methionine of the protein was in the free form in the digest.

From the above results it is evident that the role of the proteolytic inhibitor in deciding the nutritive value of raw soybean is not in diminishing the degree of availability or rate of release of methionine. It is highly probable that its action is of the nature of an antigrowth factor affecting the usefulness of proteins in general. This statement is supported by the findings of Ham, *et al.* that a purified solution of proteolytic inhibitor caused growth retardation in chicks fed on a well-balanced diet.

It is thought that, apart from the tryptic inhibitor, there may be other toxic factors associated with the raw bean which are destroyed on heating. Evidence for the existence of a separate factor apart from the proteolytic inhibitor was adduced from the following experiment. Everson, *et al.* found that the growth-promoting value of soybean protein increases to a marked extent if the bean is germinated. This observation was also confirmed here, and on examining the concentration of the proteolytic inhibitor in germinated soybean (48 hours) it was found that it was not altered from that in the original bean. The concept of the proteolytic inhibitor cannot explain this increase in nutritive value after germination. That there was no change in the amino-acid composition of the protein after germination was proved by Block, *et al.* (*2*), who could detect no change in the contents of tyrosine, tryptophane, phenylalanine, cystine, and methionine in the protein of soybean after germination.

From the above findings it can be postulated that apart from the proteolytic inhibitor there is a separate factor which affects the nutritive value of the soybean protein. Further work on the isolation of this factor and the respective roles of these inhibitors in the nutritive value of soybean is in progress.

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Effect of Benzene Hexachloride on the Flavor of Poultry Meat

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Tests conducted during the summer of 1947 show that the meat of chickens fed, sprayed, or retained in a house previously sprayed with benzene hexachloride has a distasteful flavor. This flavor, which makes the meat nearly inedible, persists for a period of 6–10 weeks.

The absorption of a benzene hexachloride flavor and odor was first discovered accidentally. In the fall of 1946 and spring of 1947 a number of chemicals were tested for the control of chicken mites. A paper on the results of these tests is in press for the *Journal of Economic Entomology*. During the course of this study several chemicals, including benzene hexachloride, showed promise, and a test to determine their toxicity to poultry was undertaken. A 5 per cent concentration of wettable benzene hexachloride containing 5 per cent of the γ isomer was applied to several chickens, the house, and the litter in December 1946. This test was concluded, and the house was not cleaned up or used until May 1947. At this time market birds were placed in the house and fed grain in the litter as well as mash in a feeder for a period of 1 week. When cooked, the meat of these birds was not edible because of a distasteful flavor apparently caused by the absorption of benzene hexachloride.

Since many manufacturers and promoters of insecticides had used and are now recommending benzene hexachloride

[1] With the cooperation of the Departments of Poultry Husbandry and Home Economics.

in poultry houses, it was decided that a determination of the manner of absorption and persistence of the benzene hexachloride flavor should be made. To this end the following test was set up. Four chicken houses were selected. In one house, 5 birds were fed for 1 week with a mixture of 1 part of benzene hexachloride containing 6 per cent of the γ isomer in 200 parts of a mash-grain feed, and then transferred to the standard ration received by the other lots. In the second house, 5 birds were sprayed until wet with a benzene hexachloride suspension containing 0.25 per cent of the γ isomer. In the third, the walls were sprayed until wet with a benzene hexachloride suspension containing 0.25 per cent of the γ isomer and allowed to dry before the birds were placed inside. In the fourth house, which was isolated from the treated lots, 5 untreated birds were retained as controls. Sprays were applied with a 3-gallon compressed-air sprayer. The birds used were 2-pound White Leghorn cockerels.

One of the birds in the lot receiving the treated feed died at the end of the first week. The bird apparently died of starvation, since the entire lot ate less than a pound of the treated feed in the 7-day period. One of the birds in the sprayed lot also died. These deaths reduced the samples from the 5 originally planned to 4. The remaining birds remained healthy until sampled and killed. The test was begun on June 13, 1947, and the final sample was taken on August 22, 1947.

TABLE 1

COMPARATIVE ABSORPTION AND RETENTION OF BENZENE HEXACHLORIDE ODOR AND TASTE BY CHICKENS

Treatments		Comparative rating of odor and taste			
		2 weeks	4 weeks	6 weeks	10 weeks
Feed treated	Odor	Slight	Moderate	Strong	Strong
	Taste	Slight	Moderate	Strong	Strong
Birds sprayed	Odor	Moderate	Strong	Strong	Moderate
	Taste	Strong	Strong	Strong	Slight
House sprayed	Odor	Strong	Slight	Slight	Slight
	Taste	Moderate	Slight	Slight	Moderate
Control	Odor	Not checked	None	Slight	None
	Taste	Not checked	None	None	None

The first 3 samples were taken at intervals of 2 weeks and the last after a 4-week interval. At sampling time 1 bird from each of the lots was killed and cooled. The following day the birds were roasted in separate ovens at uniform temperatures, no salt or other condiment being used. Five tasters or samplers then checked each bird, which was identified only by a code letter. Checks were made by smelling each of the partially carved carcasses and then tasting small pieces of white and dark meat cut from each bird. Each sampler recorded his own reaction to the quality of the particular meat.

The terms used to describe odor were very strong, strong, sharp, bad, slight, questionable and good; those used to describe taste were very strong, strong, acidic, musty, medicinal, biting, objectional, and good. The terms were modified into those used in Table 1, which gives the results of the test. Statements concerning the presence and comparative degree of an off-flavor or odor are included in the table only when the reactions of 3 or more of the samplers were the same.

In Vitro Resistance of the Genus *Bacteroides* to Streptomycin

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There is little reference to the genus *Bacteroides* in the growing literature on the *in vitro* sensitivity of various gram-negative bacteria to streptomycin. Since these microorganisms, normally saprophytic inhabitants of the nasopharynx (*16*), gastrointestinal tract (*11*), and the female genitalia (*13*), frequently invade the deeper tissues of the body to produce serious and often fatal disease in man (*19*, *20*), it seemed worth while to determine their sensitivity to streptomycin.

The obligate anaerobic, nonsporulating gram-negative bacilli comprising the genus *Bacteroides* are a heterologous group closely related to the genera *Dialister* and *Fusobacterium*. Bergey (*1*) lists 22 species of this genus, but since these have not yet been studied systematically, it is impossible to determine how many of them actually represent distinct species. Weiss and Rettger (*21*), for example, were able to classify 73 different strains into 4 serologic groups. Henthorne, Thompson, and Beaver (*14*) have reported that pleomorphic strains are serologically distinct from the nonpleomorphic strains. Therefore, following the convention adopted by Smith and Ropes (*20*), the strains reported in this study were classified as *B. funduliformis* if pleomorphic and *B. fragilis* if nonpleomorphic. Pleomorphism was determined by the formation of large bodies and filaments in artificial media and by a form of reproduction different than simple binary fission, associated with the production of anaerobic pleuropneumonia-like colonies (L-variation), as described by Dienes (*6*) and Dienes and Smith (*7–9*).

Four strains of *B. funduliformis* and 8 of *B. fragilis* have been encountered in this laboratory during the past year. These were isolated in primary culture on anaerobic horse blood or ascitic fluid agar plates, or in sodium thioglycollate broth. Subcultures were carried in chopped meat or sodium thioglycollate enriched with 30 per cent ascitic fluid and sealed with vaseline. All strains produced varying amounts of gas in these media and were characterized by a sharp, acrid odor. Strains were examined for pleomorphism and the production of anaerobic pleuropneumonia-like colonies by the cultivation and in situ agar block staining methods previously described by Dienes (*5*).

Streptomycin sensitivity was determined in unsealed 0.1 per cent sodium thioglycollate broth containing 0.1 per cent agar-agar, according to a titration based on the methods described by Price, Nielsen, and Welch (*17*). Streptomycin sulfate was diluted so that 4 times the desired doses were contained in 0.5-ml. volumes of broth. To these 0.5-ml. volumes was added 1.5 ml. of a 1:100 dilution of an 18- to 24-hour culture of the strain to be tested, giving a titration with final concentrations of streptomycin ranging from 4 0 mg. to 2.0 μg./ml. in a total volume of 2.0 ml. At the same time, each strain was tested for its ability to grow in the presence of 100 Oxford units of penicillin/ml. in the same medium. All titrations were examined after 48 hours incubation at 37°C. The first tube in which growth was inhibited was taken as the minimal inhibiting dose.

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All strains grew in the presence of 100 Oxford units of penicillin/ml. As may be seen in Table 1, *B. funduliformis* seemed to be somewhat more sensitive to streptomycin than did *B. fragilis*, although in either case the minimal doses of streptomycin required for inhibition were well beyond those usually obtainable *in vivo*.

TABLE I

In vitro RESISTANCE OF *Bacteroides* TO STREPTOMYCIN

Species	Strain No.	Source of culture	Streptomycin resistance	
			Inhibited by μg./ml.	Minimal inhibiting dose corrected for suppressive effect of thioglycollate and anaerobiosis
B. funduliformis	1	Subphrenic abscess	1,500	750
	2	Liver "	1,500	750
	3	Brain "	3,000	1,500
	4	Brain " , chronic otitis media	1,500	750
B. fragilis	5	Multiple buttocks, ischiorectal abscess	3,500	1,750
	6	Breast abscess	2,500	1,250
	7	Brain " , chronic otitis media	3,000	1,500
	8	Brain abscess, chronic otitis media	2,500	1,250
	9	Infected rectal tumor	3,000	1,500
	10	Stool	3,500	1,750
	11	"	2,500	1,250
	12	"	4,000	2,000

It has been reported that the presence of reducing substances in the medium interferes with the inhibiting action of streptomycin (*2*, *4*, *10*, *12*). Opinion differs, however, on the inhibiting effect of sodium thioglycollate. Geiger, Green, and Waksman (*12*) found that thioglycollate agar did not inhibit streptomycin, while Donovick and Rake (*10*) reported that thioglycollate broth increased the minimal concentration of streptomycin necessary for the inhibition of *Klebsiella pneumoniae*. If streptomycin reacts with the sulfhydryl compounds containing basic amino groups in the vicinity of the —SH, as has been suggested by Cavallito (*3*), its inactivation could be brought about by the active —SH groups contained in sodium thioglycollate. However, the observations of Geiger, Green, and Waksman (*12*) with facultative anaerobes suggest that simple anaerobiosis, with the consequent accumulation of acid resulting from bacterial metabolism, may suppress the inhibiting action of streptomycin by as much as 50 per cent. However, as suggested by these same authors, as well as by Bondi and Dietz (*2*), the resistance exhibited to streptomycin by anaerobic microorganisms may be the result of differences in the metabolism of the anaerobes—streptomycin may more effectively block an enzyme system essential to the growth of aerobic bacteria.

In order to determine the effect of the presence of sodium thioglycollate on the *in vitro* streptomycin resistance of *Bacteroides*, representative strains of *B. funduliformis* and *B. fragilis* were tested for sensitivity to streptomycin in tryptic digest broth containing 0.1 per cent dextrose. The medium was boiled in order to remove dissolved oxygen and streptomycin sulfate titrated as previously described. Each tube of the titration was then sealed with a thick layer of vaseline and incubated at 37°C. for 48 hours. There was no significant difference between the results obtained by this method and those obtained in sodium thioglycollate with the same strains of *Bacteroides*. It might be mentioned also that in connection with another study (*15*), successive urine cultures collected from patients receiving streptomycin therapy were cultivated in sodium thioglycollate broth as well as on the usual aerobic media. In no instance was growth obtained in sodium thioglycollate, which theoretically should have inactivated the streptomycin present in the specimen, when growth was not obtained on aerobic media as well.

With the strains reported here, even if the observed minimal inhibiting dose is reduced by 50 per cent to allow for the possible suppressive effects of sodium thioglycollate and anaerobiosis, the concentrations of streptomycin necessary to inhibit the growth of *Bacteroides* still place them in the category of highly streptomycin-resistant microorganisms. The 3 strains of *B. fragilis* isolated from stools (Table 1) were recovered from patients receiving oral streptomycin. These apparently survived exposure to the very high concentrations of streptomycin obtained in the feces following oral therapy (*18*).

In view of the resistance of these microorganisms to streptomycin, together with the possible beneficial effect of sulfadiazine in one of the cases reported by Smith and Ropes (*20*), 2 strains of *B. funduliformis* and 5 of *B. fragilis* were examined for sensitivity to sulfathiazole and sulfadiazine. These tests were done in sterile, buffered ascitic fluid under vaseline seal. With the exception of a single strain, all 7 cultures so tested grew in the presence of 10 mg. per cent of either drug. The single exception, a strain of *B. fragilis* (Strain 4, Table 1), isolated from a brain abscess secondary to chronic otitis media, was inhibited by 10 mg. per cent of sulfadiazine but not by a similar concentration of sulfathiazole.

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IN THE LABORATORY

A Method for Determining the Volume of Small Solid Objects[1]

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Frequently it is difficult to determine with accuracy the volume of small objects of unknown density, especially when the object must be kept moist. In this laboratory we found it necessary to determine the volume of a large number of teeth which could not be permitted to dry. The most logical solution to this problem appeared to be the measurement of fluid displacement. The illustration shows the plan by which the fluid displaced by the object (F) is measured in a small-bore pipette. The potential accuracy of the instrument is primarily dependent on the ratio of the volume displaced to the bore of the pipette.

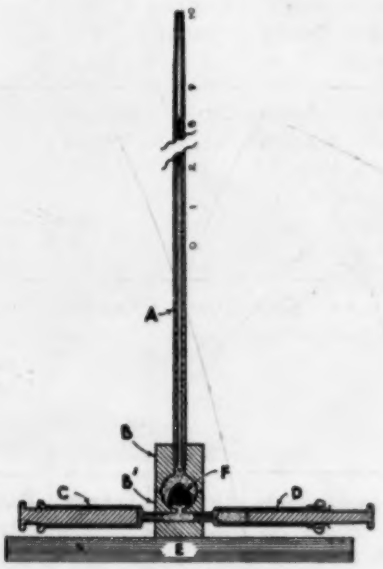

FIG. 1

The equipment consists of an ordinary graduated pipette (A), accurately faced methyl methacrylate blocks (B and B'), a large glass syringe (C), a smaller syringe (D), and a metal base (E). The syringes and the pipette are fitted into the plastic blocks through ground joints, making it possible to use various syringe combinations as well as pipettes of various sizes, provided that they are uniformly tapered. For our work, a 1-cc. pipette, a 2-cc. and a 1-cc. syringe were adequate. Stopcock grease should be used between the plastic blocks in order to prevent leakage. Volume determinations are made by filling both syringes and a portion of the lower chamber with distilled water. The upper section is then put in position and the plunger of the larger syringe inserted completely. The height of the water in the pipette is then adjusted to the zero mark by means of the smaller syringe. The plunger of the adjusting syringe should have a tension clamp to prevent free movement. Then, by withdrawing the plunger in the larger syringe, the water is removed from the upper unit and partially removed from the lower chamber. The blocks then are separated, and the object whose volume is to be determined is placed in the lower chamber. The upper unit is put in position as before, and the plunger of the large syringe is inserted completely. Since the same volume of fluid has been replaced in the system, the difference between the original height of the column and the present height is equal to the volume of the object in the chamber. The reading may be taken directly from the calibrated pipette. After each determination, the water column must be adjusted for the initial reading as described above. This method is rapid and, we believe, quite accurate. The size of the apparatus is dependent on the volume of the objects to be studied. Any fluid compatible with the materials in the apparatus may be used.

[1] From research being aided through a grant from the Sugar Research Foundation.

A Contact Culture Method for Detecting Molds on Surfaces

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A number of methods for the detection of molds on surfaces have been devised. In one of these (*2*) melted agar is placed on the surface to be tested, while in others (*1*, *3*) solidified agar is brought into contact with the surface. The method described below is of the latter type. It differs from other methods of this type in that a culture area equivalent to that in a standard-sized Petri dish is employed. The materials necessary for its preparation are readily available in the laboratory. The method has been used for culturing molds from contaminated surfaces in food plants. With the acid types of media employed yeasts also appeared on the plates, and by the choice of appropriate media the method could also be used for bacteria.

From a coarse type of filter paper discs approximately 8.5 cm. in diameter are cut, a small tab approximately 5 x 15 mm. being left on one side of each disc. The discs are soaked in a 0.5 per cent water solution of methylene blue until thoroughly colored and then rinsed in water to remove excess stain. When the rinse water is relatively free of stain, each disc is placed in a Petri dish and sterilized in the usual way by dry heat. Three ml. of melted sterile agar is added to hold the paper flat to the bottom of the plate. After cooling, 7 ml. of sterile agar, of appropriate composition to make a thin coating over the paper, is added. When the agar hardens, it is ready for use.

To test exposed surfaces in food plants for contamination with molds and yeasts, the agar-coated paper disc is removed

aseptically by grasping the tab with sterile forceps and placed carefully, face down, upon the area under test. It is then removed and replaced in the Petri dish in its original condition.

FIG. 1. Appearance of typical colonies on filter paper culture.

Mold and yeast growths may be noted in 24 hours with the Greenough microscope. Colonies usually become distinct within 48 hours. The blue paper is used merely to facilitate counting of the colonies. A typical culture is shown in Fig. 1.

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The Color Reactions of Sulfonamides With β-Naphthoquinone-4-Sulfonate

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The reaction of β-naphthoquinone-4-sulfonate with amino groups to yield colored substituted naphthoquinones may be utilized as a qualitative method of differentiation for the various sulfonamides now used in antibacterial therapy.

For the purpose of detection and identification of the pure compounds or of the compounds in pure systems, the varying colors produced by the surface reaction of β-naphthoquinone-4-sulfonate solution with an aqueous suspension of the various sulfonamides, as well as the speed of the reaction or color formation, may be a useful device.

Reactions of the naphthoquinone were noted with p-aminobenzene sulfonamide (Sulfanilamide), 2-sulfanilamido thiazole (Sulfathiazole), 2-sulfanilamido pyrimidine (Sulfadiazine), 2-sulfanilamido-4-methylpyrimidine (Sulfamerazine), 2-(N^4-succinylsulfanilamido) thiazole (Sulfasuxidine), 2-sulfanilamido guanidine (Sulfaguanidine), and 2-sulfanilamido pyridine (Sulfapyridine).

All of these compounds with the exception of Sulfasuxidine contain a primary aromatic amino group and all except Sulfaguanidine have a portion of their structure in common:

Sulfaguanidine contains no hydrogen on the sulfonyl nitrogen attached to the guanidine carbon by a double bond.

The R moiety of the molecule varies in each case and this apparently influences the color of the compound formed and the speed of the reaction.

The test is carried out by suspending approximately 100 mg. of the sulfonamide in 5 cc. of distilled water in a test tube and adding 1.0 cc. of a 0.5 per cent solution of β-naphthoquinone-4-sulfonate as the sodium salt.[1] The color formation and color change are observed during the first minute and again after 5 minutes. The addition of 5 cc. of 10 per cent ammonium hydroxide provides a confirmatory test in some instances.

TABLE 1

Compound	Color after 1 min.	Color after 5 min.	Color after addition of NH_4OH
Sulfanilamide: *stable* bright orange suspension formed within 30 seconds	Bright orange	Bright orange	
Sulfathiazole: *rapid change* from yellow through orange to a brick red in 2–3 minutes, then to a reddish brown, and finally to a *stable* purple brown	Dark orange	Purple brown	
Sulfadiazine: *very slow change* from lemon yellow	Deep yellow	Orange yellow	Clear, deep brown changing to emerald green (differentiation from Sulfamerazine); *stable* for several hours
Sulfamerazine: *rapid change* from lemon yellow to orange yellow to orange (not as dark as Sulfanilamide and changes much more slowly)	Orange	Orange	Dark orange changing to clear, dark brown (differentiation from Sulfadiazine); *stable* for several hours
Sulfasuxidine: *stable* lemon yellow	Yellow	Yellow	
Sulfaguanidine: *rapid change* from yellow to a *stable* bright crimson within 30 seconds	Crimson	Crimson	Clear brown solution (differentiation from Sulfapyridine)
Sulfapyridine: *slow change* from yellow to orange (differentiation from Sulfaguanidine)	Orange	Crimson	Brown solution rapidly changing to emerald green (differentiation from Sulfaguanidine)

Results of the test using the compounds listed are shown in Table 1. It is thus possible to identify or to distinguish between various sulfonamide compounds now commercially available for therapeutic use.

[1] Sodium β-naphthoquinone-4-sulfonate, Eastman Kodak Company.

Recording Uterine Contraction Patterns in Pregnant Women: Application of the Strain Gage in a Multichannel Tokodynamometer

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Present methods of studying uterine activity in women during the latter part of pregnancy give no indication of the pattern characteristics of the contracting uterus. Methods in use are essentially of two types. One records pressure from a single, isolated region transmitted to a tokograph which is applied to the abdomen externally (*1*). The other measures changing pressures by means of a balloon (or balloons) placed within the uterus during the course of labor.

The ideal method of recording uterine activity should yield information continuously concerning the nature of the activity in several parts of the uterus. The method described briefly below accomplishes this.

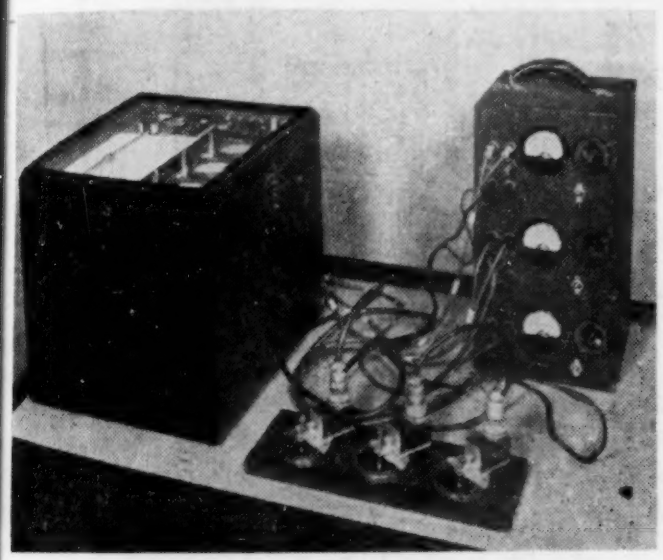

Fig. 1. Units of the multichannel Tokodynamometer. Right foreground: three strain-gage pick-up units mounted on brass rings described in text. (A later model of the dynamometer employs a smaller case and dispenses with the large plug.) Right rear: three-channel power supply and control unit. Left: frictionless writing unit containing three microammeters having insulated extensions on their pointers. Sparks, passing through a metal tip on the extension pass through the heat-sensitized paper which moves at a speed of 0.2 or 1.0 inch/minute.

The instrument which we have devised (Fig. 1) records electrically on a single piece of moving paper the uterine activity at each of three selected points on the ventral or ventrolateral aspect of the abdomen during the latter months of pregnancy. The principle employed involves application of the strain-gage dynamometer to direct electrometric recording through frictionless writing. The key to this method is the specially devised pick-up which makes it possible to apply a strain gage to the abdomen.

Pick-up device. Statham strain-gage dynamometers, Model YE-4-250, are so mounted on heavy (240-gram) brass rings that the sensitive element of the gage is connected by a simple lever system to an adjustable plunger (diameter, 7 mm.) held vertically in the center of the ring. Each of the three rings (½ inch wide; internal diameter, 47 mm.) is held in place on the abdomen by double-coated Scotch tape applied to the under side.

Power supply and circuit. The input current of each strain gage is derived from a 6-volt A battery and is controlled by a 200-ohm variable resistance, a 0.50 milliammeter, and a switch. The output from each gage goes directly to a Weston microammeter, Model 699, modified in such a way that it is balanced with a fine quartz tubing extension on its indicating arm. On the end of this is a small piece of 36-gage nichrome wire mounted vertically like a cross on a T.

Recorder. The recording unit now in use was made to our specifications by the Electro Physical Laboratories, New York City. It operates by distributing sparks through each of the three nichrome wire tips at half-second intervals. The sparks pass from a plate above to a plate below while a specially treated heat-sensitive paper passes over the lower plate at the rate of either 5 or 25 mm./minute. A heated point marks minute intervals at the bottom of the paper. The tips of the ammeters swing freely between the metal plates and over the paper without touching either, *i.e.* by frictionless writing. The instrument is so sensitive that the top of the unit is enclosed in a plastic case during recording to prevent disturbance from air currents.

The records of uterine contractility consist of a series of fine holes burned through the paper in the position under the nichrome tip according to its position at the instant of sparking. This position depends upon the amount of pressure applied to the plunger described above.

Operation. In operation, the gages are secured at the sites of choice in the manner described. The plunger is adjusted so that the needle of each ammeter is just slightly deflected. By turning a single switch on the recorder, the paper starts moving and the sparking mechanism begins to record.

To analyze the records obtained, the gages are calibrated by hanging gram weights (up to 75 grams for full-scale deflection) on the lever arm of the pick-up unit. These are noted on three scales inscribed on a sheet of Lucite in which the divisions are marked on curved lines directly over and matching the radius of curvature of the swing of the ammeter when this is recorded on stationary paper. In addition to these marks, a cut-out is made at the bottom of the Lucite plate with one side of the opening matching the time line. By placing the plastic plate over a portion of a record, the force exerted against each plunger of the pick-up may be read directly at any moment, and, in addition, time events on any one curve or the time relations between any part of the several curves may be read by appropriate marking of the record on the time line. In this way, simultaneous ordinates are automatically obtained for the three curves.

It has been ascertained recently that an ink-writing, two-channel recorder made by the Brush Development Company, Cleveland, works equally well with the pick-ups which we have devised. This unit consists of one DC amplifier for each channel (Number BL 913) and one Double Channel Magnetic Oscillograph (Number BL 202), modified by adding a slow-speed motor (10 r.p.m.).

The instrument just described has been designated a Tokodynamometer (Toko = pertaining to birth; dynamometer = measurement of force). The records obtained are *tokodynagraphs*, conveniently abbreviated TKG.

The applications of the Tokodynamometer will have to be determined by use. At present it is clear that it will serve as a tool for research in studying uterine dyskinesias, pharmacological responses of the uterus, contraction patterns in labor, and so forth. It also seems clear that it will serve as a teaching aid to student obstetricians in analyzing types of uterine activity at and near term. It is conceivable that the Tokodynamometer may prove to be of prognostic value by indicating within the limits of statistical probability the relation of the contraction pattern observed in a uterus a short time before term to the subsequent clinical course of labor.

A detailed report of the construction of this unit, including wiring diagrams, drawings, and photographs will be made at a later date in another journal.

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Freezing Points of Cobalt and Nickel and a New Determination of Planck's Constant C_2

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The International Temperature Scale (*3*) adopted in 1927 by the Seventh General Conference of Weights and Measures is based on a number of fixed points, the temperatures of which are defined. The highest temperature of these is the freezing point of gold, defined as 1,063°C. Above the gold point the temperature scale is extended by means of Wien's law of radiation. In this range any temperature, t, is determined by the ratio of intensity, J_2, of monochromatic visible radiation of wave length λ cm., emitted by a black body at temperature t, to the intensity, J_1, of radiation of the same wave length emitted by a black body at the gold point, by means of the equation:

$$\log_e \frac{J_2}{J_1} = \frac{C_2}{\lambda}\left(\frac{1}{1{,}336} - \frac{1}{t + 273}\right). \qquad (1)$$

A value of 1.432 cm.-degrees was assigned to the constant C_2. The equation is valid only if the product $\lambda(t + 273)$ is less than 0.3 cm.-degrees.

The assignment of the value 1,063°C. to the gold point was based primarily upon the gas thermometer work of Holborn and Day (*7*) and of Day and Sosman (*4*). Day and Sosman extended the constant-volume nitrogen thermometer scale up to 1,550°C. by obtaining the temperatures of various fixed points, including the freezing points of copper, nickel, cobalt, and palladium. The present authors were very fortunate to have available for this work samples of nickel and cobalt from the same lots of these materials used by Day and Sosman. Thus, the freezing points of these materials on the International Temperature Scale could be compared directly with the values determined on the gas thermometer scale. Although this comparison of temperature scales was the primary object of the present work, the samples of nickel and cobalt were of such purity that the observed values of the freezing points are the same, within observational error, as those of the pure metals.

A detailed discussion giving the sources and the analyses of the metals used by Day and Sosman in their gas thermometer work is given on page 85 of reference 4. The analyses of the nickel and cobalt ingots made at the conclusion of the present work gave essentially the same results as those originally reported by Allen, of the Geophysical Laboratory.

The so-called crucible method was used in the freezing-point determinations. In this method the radiation from a hollow enclosure or black body immersed in the molten metal is observed with an optical pyrometer as the metal freezes. In the present work the metals were melted in a high-frequency induction furnace.

Beryllia and thoria were used as crucible materials, thoria proving more satisfactory because of its greater mechanical strength. Freezing-point determinations were made in an atmosphere of helium and *in vacuo*, since both metals oxidize readily at high temperature.

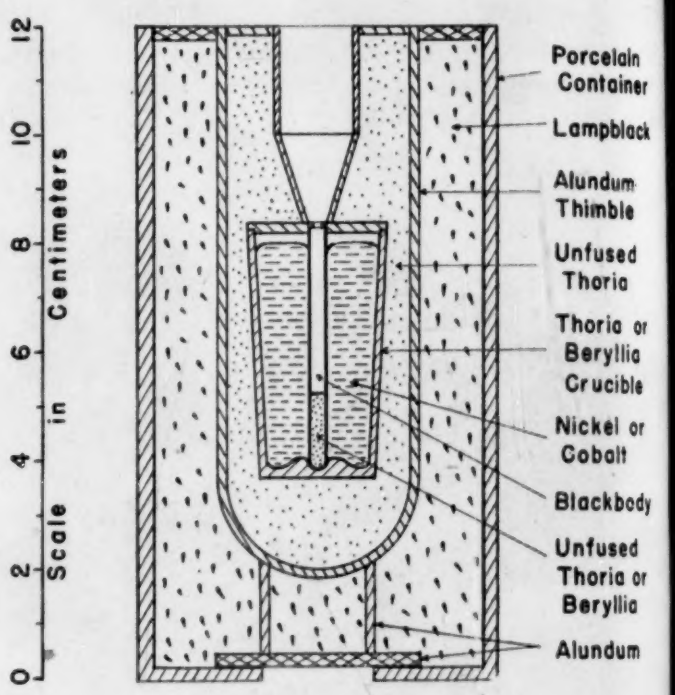

FIG. 1

Fig. 1 is a cross-sectional view of the crucible assembly. The 80-gram samples of nickel and cobalt were first melted in beryllia crucibles of the size and shape to be used in the freezing-point determinations. A hole was drilled axially in each ingot to accommodate the sight tube. The sample and its sight tube were placed in a refractory-oxide crucible and mounted in a larger porcelain container, as shown. The relatively coarse insulating material surrounding the crucible permitted the passage of gas around the sample, while the lampblack provided excellent thermal insulation. The assembly shown was placed inside a closed Pyrex tube having a Pyrex window sealed to the top with propylene phthalate. The Pyrex tube fitted closely inside the water-cooled coil of the induction furnace.

Before melting the sample in a helium atmosphere, the gas was passed slowly through the Pyrex enclosure for about 16 hours before heating, as well as during the actual heating. For the experiments *in vacuo*, the pressure within the enclosure was maintained less than 0.005 mm. of mercury by a mercury diffusion pump. A liquid-air trap between the diffusion pump and

e Pyrex tube prevented mercury vapor from entering the be.

The optical pyrometer used was designed by Fairchild and oover (*5*). It was fitted with a 45° total-reflecting prism for ghting into the black body. Two separate pyrometer lamps ere used during the investigation. For observations on the lack body at the gold point, an assembly of the same dimenons as that shown in Fig. 1 was used.

The brightness ratio, J_2/J_1, was measured by utilizing a roating sector disk. The sector had two openings and was made y mounting steel strips on an aluminum disk. The edges of he strips were ground, and lapped straight and aligned to be adial with the aid of a circular dividing engine. The transission of the sector, as computed from the measurement of he openings with a circular dividing engine, was 2.625 per ent.

In addition to using the sector disk, an absorption glass was sed to obtain temperature measurements at the freezing oints of the metals. This had been calibrated repeatedly by

TABLE 1

Lamp No.	Absorption device	Nickel		Cobalt	
		No. of freezes	Avg. value of freezing point(°C.)	No. of freezes	Avg. value of freezing point(°C.)
-16	Glass	10	1,455.0	22	1,494.7
-16	Sector	29	1,455.3	13	1,494.8
-1	Glass	18	1,455.3	22	1,494.4
-1	Sector	7	1,455.0	4	1,495.3
Weighted mean			1,455.2		1,494.7

comparison with sector disks over a period of about 20 years, nd the calibration is considered well established.

About 60 freezes on each metal were made, with both uthors serving as observers. The average number of pyrometer settings during one freeze was 7. About 10 freezes on each metal were made with the samples *in vacuo* and the remainder with the samples in helium. No significant differences were noted.

A summary of the determinations of the freezing points of nickel and cobalt obtained by use of equation (1) is given in Table 1.

In view of estimated uncertainties, the best values of the freezing points are taken as 1,455 ± 1°C. for nickel and 1,495 ± 1°C. for cobalt.

The ratios of brightness (J_2/J_1) of black bodies at the freezing points of nickel and cobalt to that of a black body at the gold point were found to be as follows: for nickel, where $\lambda = 0.6533\mu$, $J_2/J_1 = 41.40$; and for cobalt, where $\lambda = 0.6532\mu$, $J_2/J_1 = 54.99$.

Using the values of the freezing points of gold, nickel, and cobalt as determined by Day and Sosman, and the above values of the ratios of brightness, values of the constant C_2 in Planck's law of radiation can be calculated. For simplicity, Wien's law is used in the calculations, since it gives essentially the same numerical results as Planck's law in the temperature range investigated. Since the values of Day and Sosman for the temperatures of the various fixed points are on the constant-volume nitrogen scale, small corrections are necessary to convert them to the thermodynamic scale (*2*, *8*).

Wien's law yields the following expression for C_2:

$$C_2 = \frac{\lambda \log_e \frac{J_t}{J_{Au}}}{\frac{1}{t_{Au} + 273} - \frac{1}{t + 273}}. \qquad (2)$$

In addition to the samples of nickel and cobalt used in the present work, Fairchild, Hoover, and Peters (*6*) have measured J_t/J_{Au} for a sample of palladium, which was compared with the palladium used by Day and Sosman and found to have the same freezing point to about 0.1°C. Table 2 lists the values of C_2 as derived from these points.

Since the adoption of the International Temperature Scale there has been considerable evidence to indicate that the value assigned to C_2 is low. The International Conference of Weights and Measures was scheduled to consider revision of the temperature scale in 1939, but failed to meet because of unsettled political conditions. One of the proposed revisions was to increase the value of C_2 to 1.436 cm.-degrees. Since 1939 there has been additional evidence that the value should be still higher.

TABLE 2

VALUES OF C_2 BASED UPON OPTICAL AND GAS THERMOMETRY

Fixed point	Temperature D&S gas scale (°C.)	Thermodynamic scale (°C.)	$\text{Log}_e \frac{J_t}{J_{Au}} \times 10^7$	C_2 (cm.-degrees)
Au	1,062.4*	1,062.6		
Ni	1,452.7*	1,453.1	2,433	1.436_4
Co	1,490.6*	1,491.0	2,618	1.439_8
Pd	1,549.4*	1,549.8	2,879	1.438_2
Mean				1.438

* These values are the unweighted means of the individual determinations of Day and Sosman and are slightly different from the weighted means reported by those authors.

Values of the constant C_2 may be computed by a number of methods. Wensel (*9*) discusses these methods and summarizes the values of C_2 as obtained from the various sources. The particular value of C_2 which was given the greatest weight was that derived from the atomic constants. In the most recent summary of the physical constants, Birge (*1*) concludes that C_2 equals 1.4384_3 cm.-degrees. Thus, the present results add to the evidence that the most probable value of C_2 is 1.438 cm.-degrees.

A more detailed paper on this subject will be published in the *National Bureau of Standards Journal of Research*.

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Book Reviews

Adolescent sterility: a study in the comparative physiology of the infecundity of the adolescent organism in mammals and man. M. F. Ashley Montagu. Springfield, Ill.: Charles C. Thomas, 1946. Pp. ix + 148. (Illustrated.) $3.50.

Any contribution to the understanding of the problem of human sterility is of considerable importance, for sterility in the human seems to be increasing. Prof. Montagu has made such a contribution in this volume. He brings together evidence from both comparative (mammalian) and human physiology that the onset of menstruation does not coincide with the ability to conceive. It is this interval between the first menstrual period and the first conception that is known as the period of adolescent sterility. Ovulation is not associated with the first menstruation, but follows sometime later, the number of years varying considerably in any given population. The physiological basis for the period of adolescent sterility is hormonal control. The mechanism that starts and maintains menstruation is not the same as that which initiates ovulation, the latter being the later and more mature function. During the interval between the first menstruation and the first ovulation the organism does not remain static, but matures the sexual equipment essential for the process of reproduction.

Prof. Montagu's book is most highly recommended to every physician whose practice involves obstetrics, gynecology, and endocrinology.

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Curare: its history, nature, and clinical use. A. R. McIntyre. Chicago: Univ. Chicago Press, 1947. Pp. vii + 240. (Illustrated.) $5.00.

Curare, the arrow poison of South America, is as scientifically interesting and exciting to the biologists of today as it was intriguing to the early explorers who discovered it and the natural philosophers who first wrote accounts of it. In the large scientific literature on this subject which is added to monthly there is at present no single publication of broader scope or more profound learning on the subject than the present study. Dr. McIntyre and his associates during the last 6 years have accomplished a large amount of experimentation on the physiological and pharmacological effects of curare. In this volume he not only undertakes to place all of this experimental material, including the work of others, in an orderly review, but also provides a very scholarly historical background for the whole subject. In developing the history of curare he has been able to correct numerous errors and false impressions. He shows the relation of this and other poisons to the beginnings of modern toxicology and the development of modern physiology. Numerous quotations have been included from several of the earlier, more significant accounts, particularly from witnesses who observed the preparation of the poison extracts which were to be used by the Indians in the Amazonian jungles.

Historical notes and references occur throughout the volume, but the major portion of the book is devoted to the presentation of a wide range of experimental work. Full chapters on the botanical and chemical aspects of curare are provided, tracing these lines of study from earliest times up to the present. Other chapters cover: nerve and muscle, circulation and respiration, the viscera, the central nervous system, absorption and excretion, and toxicity. There is a chapter on theories of curarization and one entitled "Miscellaneous Effects of Curare."

Laboratory studies already completed demonstrate that curare can be used successfully in connection with shock therapy to control and prevent trauma and is useful as an adjuvant in anesthesia. Details are given for the administration of the drug for these purposes, and the anticipated clinical results are discussed. Dr. McIntyre proposes areas where new or more extensive experimentation with curare appears to offer promise of developing further therapeutic uses. The work is noteworthy also as a bibliography on curare, since each chapter contains full references to the authors cited, and these pages make up nearly 25 per cent of the total. Subject and author indexes are very adequate. The University of Chicago Committee on Publications in Biology and Medicine has sponsored this book.

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Injection molding of plastics. Islyn Thomas. New York: Reinhold, 1947. Pp. viii + 534. (Illustrated.) $10.00.

Although the first patent on an injection molding machine was granted in 1878, this is the only comprehensive book to be published on the subject. The first part of the book is devoted to the history of injection molding, giving a detailed description of many of the commercial machines, both past and present; the characteristics of thermoplastic molding powders, information which the molder can use as a basis for selecting the proper plastic; general techniques and guiding principles for the molding of different types of thermoplastic materials; recommendations for laying out a molding plant, including a description of the necessary auxiliary equipment, storage space, utility requirements, etc. The latter half deals with mold design and construction, product design and finishing, cost estimation, and finally ends with tables on the physical properties of plastics.

The text is written in language which both the layman and engineer can understand; the hundreds of illustrations serve to increase its instructiveness. Very few references are quoted other than Modern Plastics although a good portion of the data, it appears, has been taken from trade literature. The author has rendered a valuable service in selectively assembling so much authoritative information on injection molding. His treatise should help ease many of the costly headaches involved in gaining experience in the molding field.

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